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# Two-Component, Four Reaction Domino Sequence toward Novel Tricyclic 1,4-dihydro-2H-benzo(f)sochromenes

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# Two-Component, Four Reaction Domino Sequence toward Novel Tricyclic 1,4-dihydro-*2H*-benzo[*f*]isochromenes

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# APPROVAL PAGE

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# ABSTRACT

The synthesis of complex molecules usually requires multiple reactions and purification protocols for each step of the sequence. In efforts to reduce the formation of toxic byproducts, increase atom economy as well as efficiency of overall synthetic processes, we developed a one-pot, two-component reaction cascade between alkynediols and aldehydes to rapidly form tricyclic molecules. The reaction cascade between an alkynediol and aldehyde includes four different reactions: (a) intermolecular addition, (b) intramolecular alkynyl-Prins cyclization, (c) Friedel-Crafts arylation, and (d) dehydration to furnish tricyclic benzo[*f*]isochromenes. The overall process can be initiated by Lewis or Brønsted acids and the effects of electron-donating and electron-withdrawing groups on the aromatic ring of the alkynediol were examined, as were aliphatic and aromatic aldehyde reaction partners. An alkynediol containing a defined stereocenter led to two diastereomeric products that were each enantiomerically-pure. The final benzo[*f*]isochromene products were characterized by IR and NMR spectroscopy, HPLC, GC and HRMS analyses and the structural assignment of two isochromenes was verified by X-ray crystallographic analysis.

# TABLE OF CONTENTS

# ACKNOWLEDGEMENTS

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# LIST OF TABLES

# LIST OF FIGURES

# CHAPTER 1. INTRODUCTION

## 1.1 COMPARISON OF STRATEGIES TOWARD HETEROCYCLE SYNTHESIS

Heterocycles are found in a wide variety of natural products.[1] In particular, tetrahydrofurans (THFs), tetrahydropyrans (THPs), dihydropyrans (DHPs), thiapyrans and piperidine scaffolds are common heterocycles. Over the years, there have been a number of elegant methodologies toward the synthesis of those heterocycles,[2] among which the Prins-type cyclization has been proved to be a powerful synthetic strategy.[3]

For example, (+)-Neopeltolide (**Figure 1.1**) has an oxygen-containing heterocycle structure. It was isolated from a deep-sea Caribbean sponge by Wright and co-workers in 2007.[4] One key structural moiety of (+)-neopeltolide is a 14-membered lactone ring, which also contains a tri-substituted tetrahydropyran ring. More than 20 papers were published related to the total synthesis or formal synthesis of Neopeltolide, applying various synthetic strategies to construct the tetrahydropyran ring, as shown below. However, many of the syntheses did rely upon the Prins cyclization to assemble the tetrahydropyran moiety.[5]

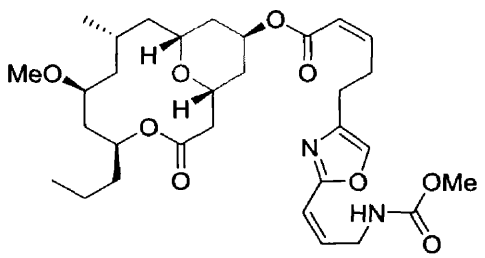
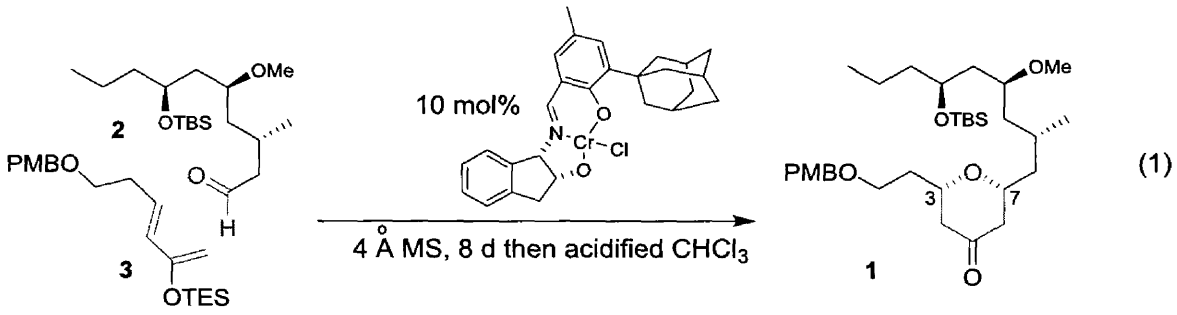



**Figure 1.1.** Structure of (+)-neopeltolide

### 1.1.1 HETERO DIELS-ALDER REACTION TOWARDS (+)-NEOPELTOLIDE

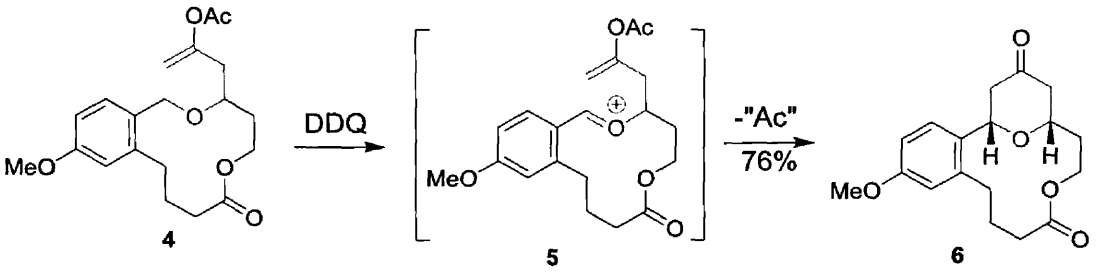
In 2008, Paterson and co-workers reported an approach towards the expected *cis*-tetrahydropyran **1** through a Jacobsen asymmetric hetero Diels–Alder reaction (eq 1),[6] which is a [4+2] cyclization addition between aldehyde dienophile **2** and silyloxy diene ether **3**, in presence of catalytic amount of chiral tridentate chromium(III). This reaction affords complete control of stereochemistry at C3 and C7 in 78% yield; however it required 8 days to reach completion.




(1)

### 1.1.2 CYCLIC ETHER OXIDATION TOWARDS (+)-NEOPELTOLIDE

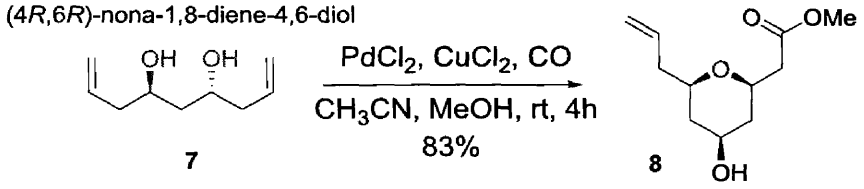
In 2010, Floreancig and coworkers examined preparing the tetrahydropyran core in (+)-neopeltolide (eq 2) via an oxidative process.[7] They employed DDQ to oxidize the benzylic ether of the inert ether **4** to form an oxocarbenium ion **5**, which was attacked by the pendent acylated enol to form tetrahydropyran **6** with excellent stereocontrol.




(2)

## 1.1.3 ALKOXYCARBONYLATION TOWARDS (+)-NEOPELTOLIDE

In 2011, She and coworkers reported a palladium-catalyzed intramolecular alkoxycarbonylation to assemble the tetrahydropyran core of (+)-neopeltolide (eq 3).[8] Treatment of chiral diol **7** with Pd(II), and Cu(II) in the presence of MeOH and carbon monoxide resulted in intramolecular alkoxycarbonylation to afford tetrahydropyranyl ester **8** in 83% yield. This step is quick and productive; however an enantiomerically-pure diol precursor was required to stereoselectively assemble *cis*-tetrahydropyran ring **8**.

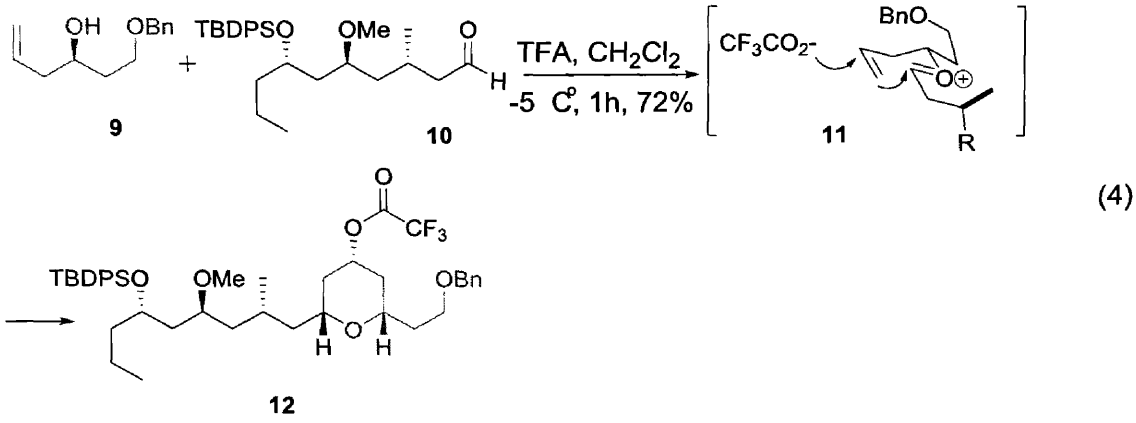



(3)

## 1.1.4 PRINS CYCLIZATION TOWARDS (+)-NEOPELTOLIDE

In 2008, Maier and co-workers developed a TFA-mediated Prins cyclization to assemble the Pyran structure in (+)-neopeltolide (eq 4).[9] The homoallylic alcohol **9** was treated with aldehyde **10** to yield the desired tetrahydropyran structure **12**. Another isomer other than the major product

(major/minor= 8:1) was also obtained. The oxocarbenium ion **11,** which adopts a chair-like conformation with the side chains and nucleophile oriented in equatorial positions, was generated as an intermediate.




(4)

Among the above syntheses (eqs 1-4), both Floreancig and Maier employed oxocarbenium ions as intermediates to furnish the tetrahydropyran core of (+)-neopeltolide with excellent stereocontrol. Strategies using oxonium ion intermediates in (+)-Neopeltolide syntheses were also applied by other investigators, such as Panek in 2007,[10] Lee in 2008,[11] Kozmin in 2008,[12] Scheidt in 2009,[13] and Florence in 2010.[14]

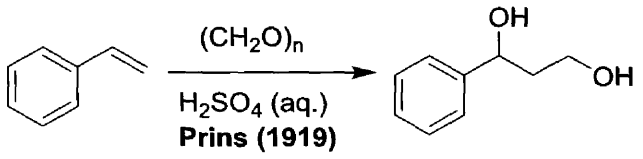
A wide variety of natural products have heterocycles in their structures, and a range of synthetic strategies have been developed to assemble the ether ring: (a) hetero Diels–Alder reaction, (b) oxidation, (c) ring closing metathesis, (d) alkoxycarbonylation, and (e) Prins cyclization. Prins cyclization, however, has been one of the most efficient approaches toward heterocycles, by allowing cylclization with excellent stereocontrol and flexible

substituent installation. The following section highlights a brief review of Prins cyclizations.

## 1.2 A BRIEF REVIEW OF PRINS CYCLIZATIONS

### 1.2.1 DEVELOPMENT AND KEY FEATURES OF PRINS CYCLIZATIONS

The Prins reaction was first reported by Dutch chemist Hendrik Jacobus Prins.[15] The original reaction was published in 1919 (eq 5), in which styrene was reacted with paraformaldehyde to afford a diol in the presence of aqueous sulfuric acid.

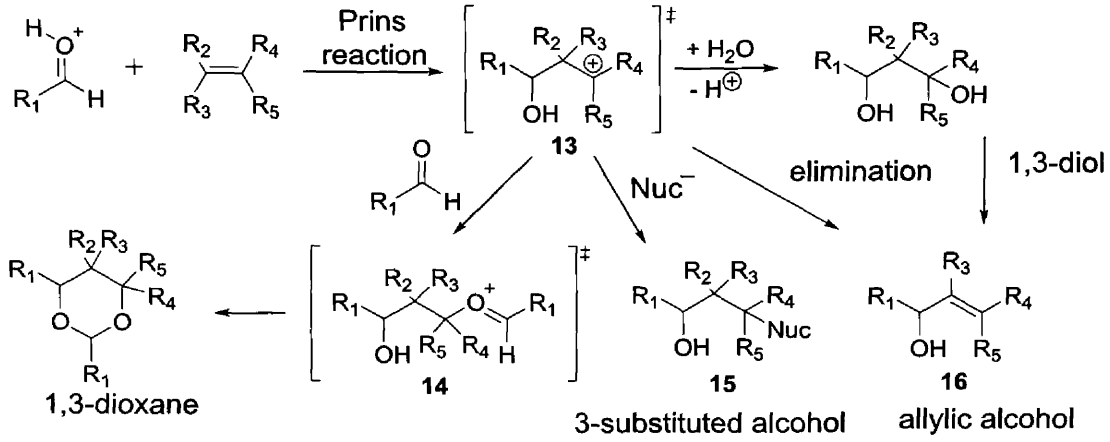



(5)

Prins reactions can generate different products depending on the reaction conditions. Scheme 1.1[16] shows a Prins reaction between an activated aldehyde and an alkene. This Prins reaction affords the initial intermediate cation **13**, which can further react with different reagents to produce various products. For example, the cationic intermediate **13** can react with aldehyde to form another oxocarbenium ion intermediate **14** to generate a 1,3-dioxane, **13** can be attacked by a nucleophile to afford substituted alcohol **15**, or proceed through an elimination reaction to generate a homoallylic alcohol **16**.

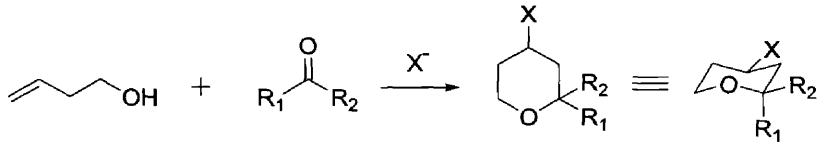
The prototypical Prins reaction is typically between aldehyde and alcohol to form an oxocarbenium ion intermediate, followed by the addition of

**Scheme 1.1.** Prins reaction and possible pathways




a π-nucleophile to generate oxygen-containing heterocycles. Also, analogous reactions are reported such as addition of nucleophile to iminium ions or thiocarbenium ions, all of which are accepted as Prins-type reactions.

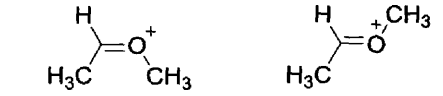
The first selective synthesis of a tetrahydropyran by Prins cyclization was achieved by Hanschke in 1955 (eq 6).[17] A homoallylic alcohol was reacted with ketone or aldehyde to quickly form the tetrahydropyran ring. Since then, the Prins cyclization has proved to be a valuable strategy towards heterocycles and has been widely used in natural products synthesis.




(6)

The configuration of the heterocycle is dependent on the geometry of the oxocarbenium ion intermediate (**17** or **18**). Houk and coworkers published their conformational analysis of oxonium ions by *Ab initio* molecular orbital

calculations in 1991.[18] Their study found that the *cis* isomer of oxocarbenium ion, **17**, was 2.0 kcal/mol less stable than the *trans* isomer, **18** (Figure 1.2), which indicates that the C=O bond has a preference for the *E*- geometry over *Z*-geometry.



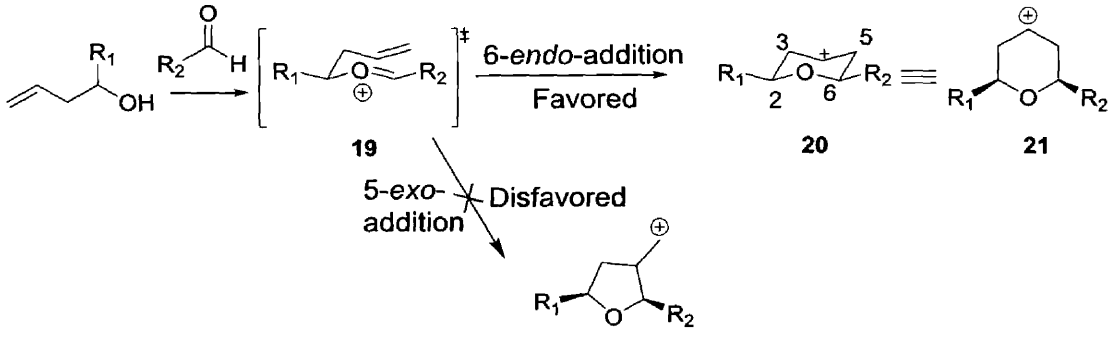

**17** cis (*Z*) $E_{rel}$ = -2 Kcal/mol

**18** trans (*E*) $E_{rel}$=0

**Figure 1.2.** Conformational analysis of oxocarbenium ions

As illustrated before, the π-nucleophile component would attack the oxocarbenium ion intermediate **19** in the Prins cyclization (**Scheme 1.2**). Once the intermediate oxocarbenium ion is formed, there are two possible pathways including *endo* and *exo* additions. For homoallylic alcohols, the Prins-type cyclization favors 6-*endo*-addition to tetrahydropyrans over 5-exo-addition to tetrahydrofurans.[19] During the *endo*-addition, substituents tend to

**Scheme 1.2.** Stereocontrol in Prins-type reactions



occupy the pseudoequatorial positions adjacent to oxygen in chair-like conformation **20** to produce *cis*-fused product **21**.[20] This overall model for cyclization is useful in designing the syntheses of poly-substituted tetrahydropyrans.

Generally, the Prins cyclization involves the following components: an electrophilic ion, a π-nucleophile, an acid promoter and a nucleophile to terminate the cyclization. Over the years, Prins cyclization has been significantly broadened, and variations were developed:

*The electrophilic component.*

The oxocarbenium ion, which can be generated from a homoallylic alcohol, homopropargylic alcohol, acetal, mixed acetal, α-acetoxy ether, enol ether, esters, and by some oxidation methods, is the typical electrophile. The aza-Prins cyclization, which uses an iminium or *N*-acylimin-ium ion as the electrophile, and the thia-Prins cyclization, which uses thiol compounds as precursors, are analogous Prins-type reactions.

*The π-nucleophile.*

Various π–nucleophiles can be employed in the Prins reaction, including alkynes, alkenes, aromatic rings, allylsilanes, and enolsilanes. The silylated nucleophiles are used because of the stabilizing influence of the silane on the cationic intermediates generated during the reaction.[27d,32]

*Acid activators.*

Both Lewis and Brønsted acids are suitable for Prins cyclizations. Lewis acids such as $FeX_3$, $SnX_4$, TFA, TMSOTf, $BF_3{\bullet}OEt_2$ and $In(OTf)_3$ are commonly used; Brønsted acids such as trifluoromethanesulfonic acid (TfOH) and camphorsulfonic acid (CSA) are also used to activate Prins reactions.

*Termination nucleophiles.*

The nucleophiles added to terminate Prins cyclizations include good nucleophiles such as halogens, allylsilanes, silyl acetates, and trimethylsilyl halides. Neutral molecules have also been used in tandem processes, and these processes include Prins/Friedel-Crafts and Prins/ Ritter reactions.

## 1.2.2 ALKENYL OXO-PRINS CYCLIZATION

The oxocarbenium ion is the most commonly used electrophilic component in Prins cyclization. It can be further reacted with an alkene in an alkenyl-Prins cyclization. Maier and co-workers' synthesis towards (+)-neopeltolide (eq 4) is an example of alkenyl oxo-Prins cyclization. As previously mentioned, this type of Prins cyclization favors 6-*endo*-addition to tetrahydropyran over 5-*exo*-addition to tetrahydrofurans. The 6-*endo*-addition to tetrahydropyrans prefers a chair-like conformation, an *E*-geometry of carbon-oxygen double bond, and equatorial orientation of substituents

adjacent to oxygen, leading to a *cis* relationship between substituents adjacent to oxygen in tetrahydropyrans.

### 1.2.3 ALKENYL AZA-PRINS CYCLIZATION

Nitrogen-containing heterocycles are important subunits of many pharmaceutical products.[21] For example, piperidine, pyrrole, indole, quinoline, decahydroquinoline and octahydroindole (**Figure 1.3**) are common nitrogen-containing heterocycles, and are core motifs of many natural products.

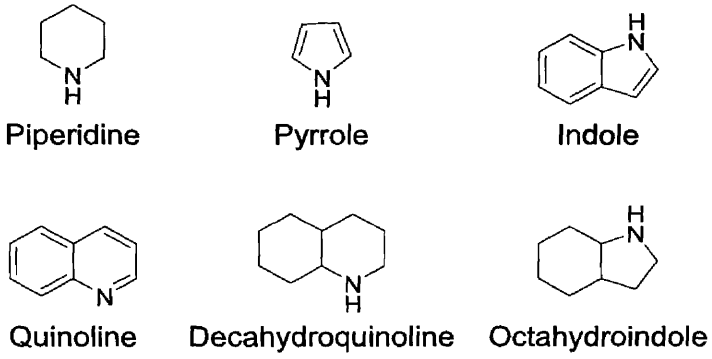


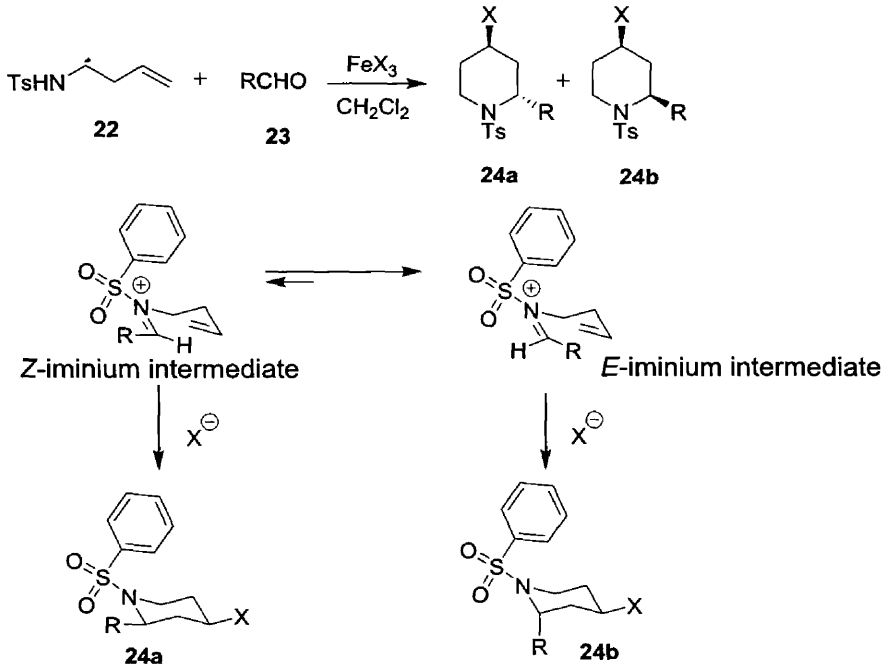

**Figure 1.3.** Nitrogen-containing heterocycles

The aza-Prins reaction is an efficient synthetic way to produce nitrogen-containing heterocycles. The aza-Prins reaction can be initiated from iminium ion, acyliminium ion and *N*-acyloxyiminium ion. The *N*-acyliminium ion chemistry is also known as a Mannich-type condensation, which is widely used to install substituents onto amines.[22] Similar to the oxo-Prins reaction, the aza-Prins cyclization involves intermolecular or intramolecular attack of a

nucleophile onto an *N*-acyloxy or *N*-substituted iminium ion generated in the presence of Lewis acid or protic acid.

Padron and coworkers[23] investigated the iron(III) halide-promoted aza-Prins cyclization between *γ,δ* -unsaturated tosylamines **22** and aldehyde **23**. They found that this aza-Prins reaction generated the *trans*-diastereomer **24a** as the major product (**Scheme 1.3**). The *E*-iminium intermediate was found to be more stable than the *Z*-iminium intermediate when R is an alkyl group; the opposite result is observed when R is an aromatic group. In both cases, the

**Scheme 1.3.** Cylization of homoallylic tosyl amine with an aldehyde, and proposed Intermediates.




most stable isomer is a result of *endo* attack of the alkene on the tosyl-iminium ion; this is the same rule as observed in the oxo-Prins reaction.

## 1.2.4 ALKYNYL OXO-PRINS CYCLIZATION

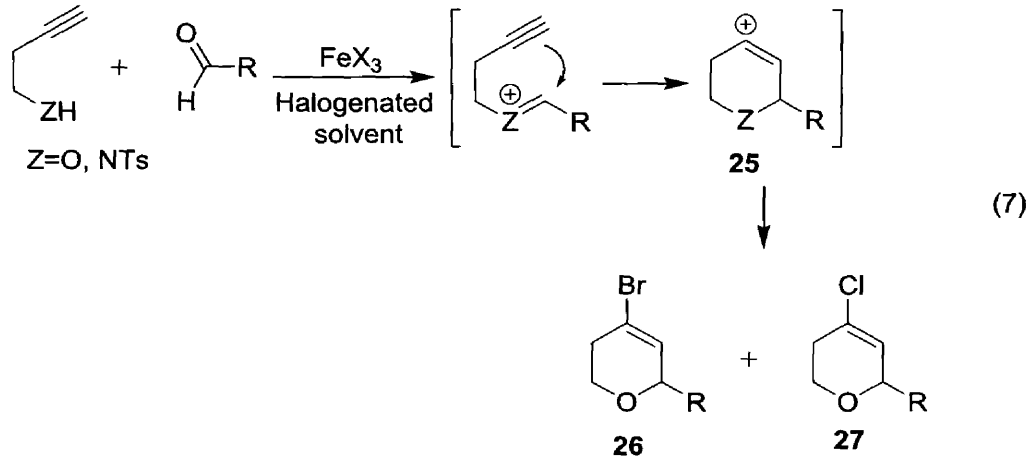
In addition to the alkenyl Prins cyclization which utilizes a phenyl group or alkene as a nucleophile, the alkynyl Prins reaction uses an alkyne as a nucleophile. The alkynyl oxo-Prins reaction plays an important role in accessing dihydropyrans (DHPs), or poly-substituted THFs[24,25a]. Research on the oxo-alkynyl Prins reaction revealed a number of trends:

1. Halogen exchange occurred with halogenated solvents in Fe(III)-promoted Prins cyclizations.[24]
2. The 2-oxonia-[3,3]-sigmatropic rearrangement competes with direct attack of the alkyne and alkenyl cation formation.[26]
3. The alkynyl-Prins reaction is an efficient method to make poly-substituted tetrahydrofurans directly. [25]

*1. Halogen exchange with halogenated solvents in iron(III) promoted Prins cyclizations[24].*

Padron's group published a paper in 2007[24b] introducing a Prins-type cyclization between homopropargylic alcohols or homopropargyl tosyl amines and aldehydes, in presence of iron (III) halides. They found an unexpected halogen abstraction by vinyl cation **25** when $FeX_3$ or $InX_3$ was used as the Lewis acid and $CH_2X_2$ as the solvent (eq 9). As a result, they obtained a mixture of **26** and **27** in $FeBr_3$ promoted Prins cyclization in $CH_2Cl_2$. They also

found that stoichiometric amount of iron (III) halides are required to generate significant amounts of halide exchange.

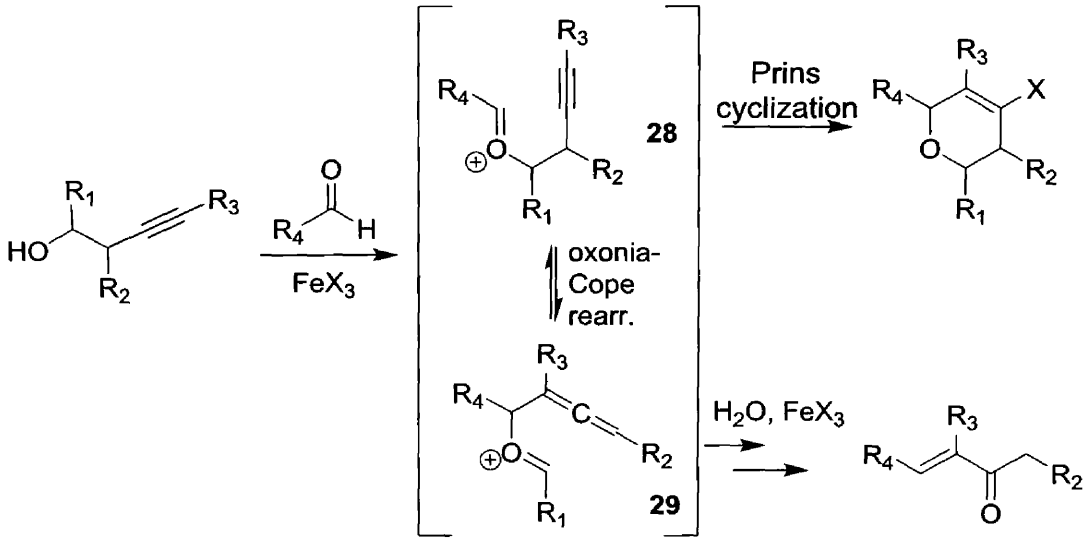



(7)

*2. The 2-oxonia-[3,3]-sigmatropic rearrangement is the main process competing with Prins cyclization.*[26]

The oxonia-Cope rearrangement is the main reaction competing with cyclization according to studies by several research groups (**Scheme 1.4**).[26a,27] The relative stabilities of intermediates from both Prins cyclization and oxonia-Cope rearrangement were studied by Padron and coworkers.[27d] In some Prins cyclizations, the oxonia-Cope rearrangement occurred only when oxocarbenium ion **29** was either lower in energy than the initial ion **28**, or if the ions were of similar energies and only a small transition state energy barrier was present between the forms.

**Scheme 1.4.** Prins cyclization and oxonia-Cope rearrangement



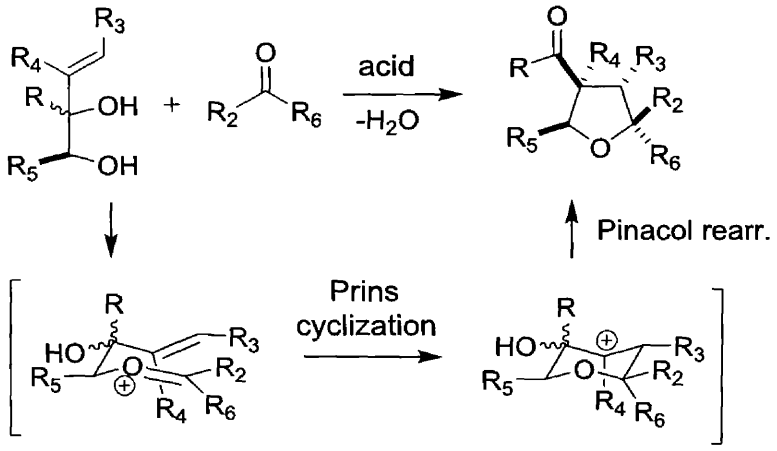

There are several factors affecting the stability of **28** and **29** such as the nature of $R_1$, $R_3$ and $R_4$ groups. Padron and coworkers' study revealed several effects related to substituents: (a) as the bulkiness of $R_4$ group increases, the Prins cyclization is more favorable than oxonium-[3,3]-sigmatropic rearrangement; (b) when TMS group was introduced at $R_3$ position, the oxonium-[3,3]-sigmatropic rearrangement was less favored; (c) electron-withdrawing groups in $R_1$ destabilize the allenic oxocarbenium ion **29**.

3. *The alkynyl-Prins reaction is an efficient method to afford poly-substitutes tetrahydrofurans.*[25]

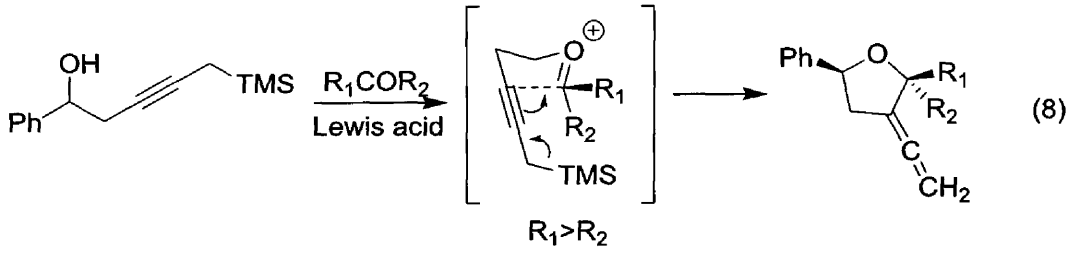
A variety of natural products such as (+)-Citreoviral, (±)-Kumausallene and Cladiellin diterpenes have an oxacyclic motif,[28] many of which are

polysubstituted tetrahydrofurans. In order to prepare the racemic or optically pure products, some groups have been putting efforts toward utilizing an alkenyl Prins cyclization followed by Pinacol rearrangement of the incipient cation (**Scheme 1.5**).[29]

**Scheme 1.5.** Pinacol-terminated Prins cyclization




The alkynyl Prins cyclization, however, can be used for synthesis of tetrahydrofurans without a Pinacol rearrangement. The alkynyl Prins cyclization affords polysubstituted tetrahydrofurans by 5-*exo* cyclization to THFs rather than 6-*endo* cyclization to DHPs. For example, Cho and coworkers reported a Prins cyclization for the stereoselective synthesis of 2,5-*cis*-disubstituted 3-vinylidene tetrahydrofurans (eq 8).[25 a]



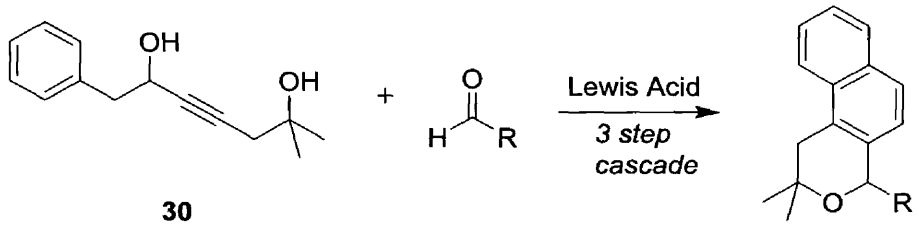

(8)

In summary, the alkynyl Prins cyclization has emerged as a powerful tool to the synthesis of polysubstituted heterocycles with six- or five-membered rings in moderate to high yields with excellent stereoselectivity.

# CHAPTER 2. RESULTS AND DISCUSSION

## 2.1 GENERAL INFORMATION ABOUT REACTIONS

To expand the scope of Prins-type reactions, Hinkle and Lewis[30] reported a reaction cascade involving an alkynyl-Prins cyclization, Friedel-Crafts arylation, and dehydration/aromatization toward tricyclic isochromenes (eq 9).

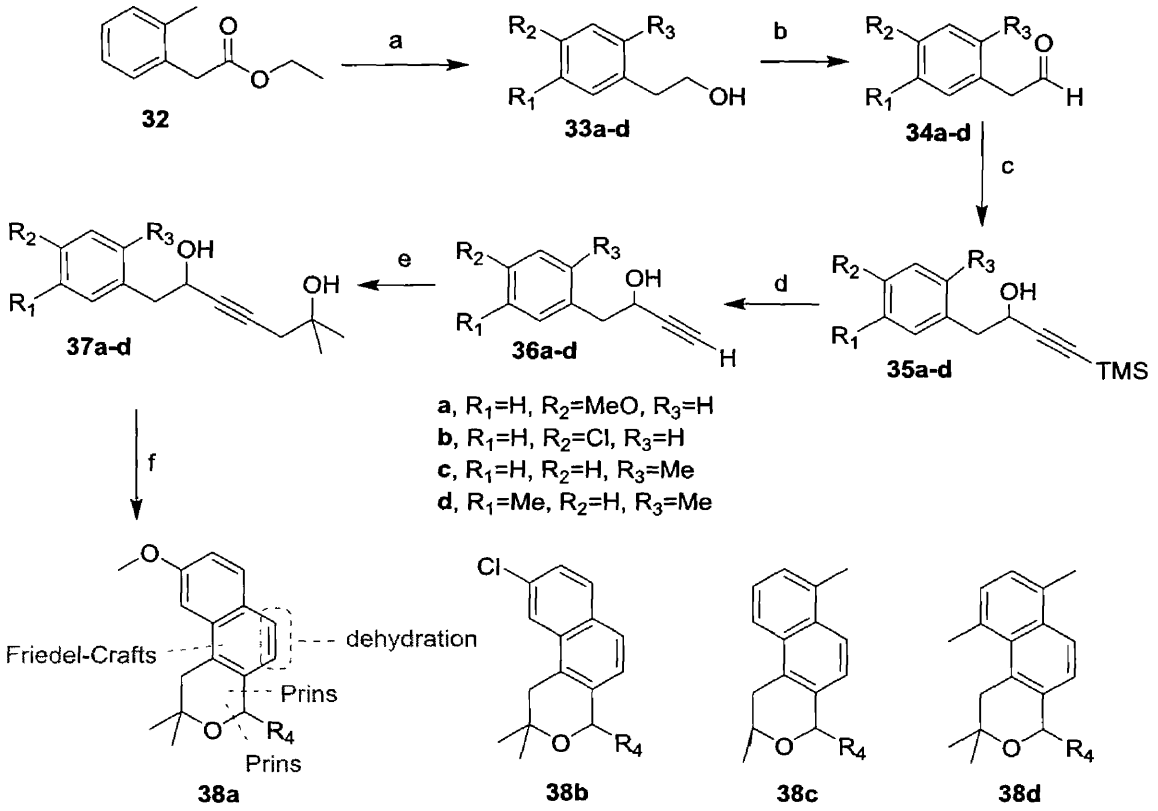



**30** **31** (9)

Based on the moderate yields obtained in the above domino reaction,[30] more research was conducted to increase yields and explore the mechanism. In order to further study the intramolecular Friedel-Crafts reaction to the alkenyl cation that is presumably generated during the alkynyl-Prins cyclization, both electron donating and withdrawing groups were introduced into the aromatic moiety of alkynediol **37**. To further understand other parts of the sequence and optimize the final yields, the effects of the following were also investigated: (a) both aromatic and aliphatic aldehydes were employed as the second reactant; (b) different Lewis acid/Brønsted acid activators were surveyed; (c) various ratios of reaction components were investigated; and (d) solvent effects were evaluated. **Scheme 2.1** outlines the entire synthetic route

from commercially available ester **32** or alcohols **33a, 33b** and **33d** toward the final tricyclic benzo[*f*]isochromenes **38**.

**Scheme 2.1.** Synthesis of different tricyclic benzo[*f*]isochromenes.[a]

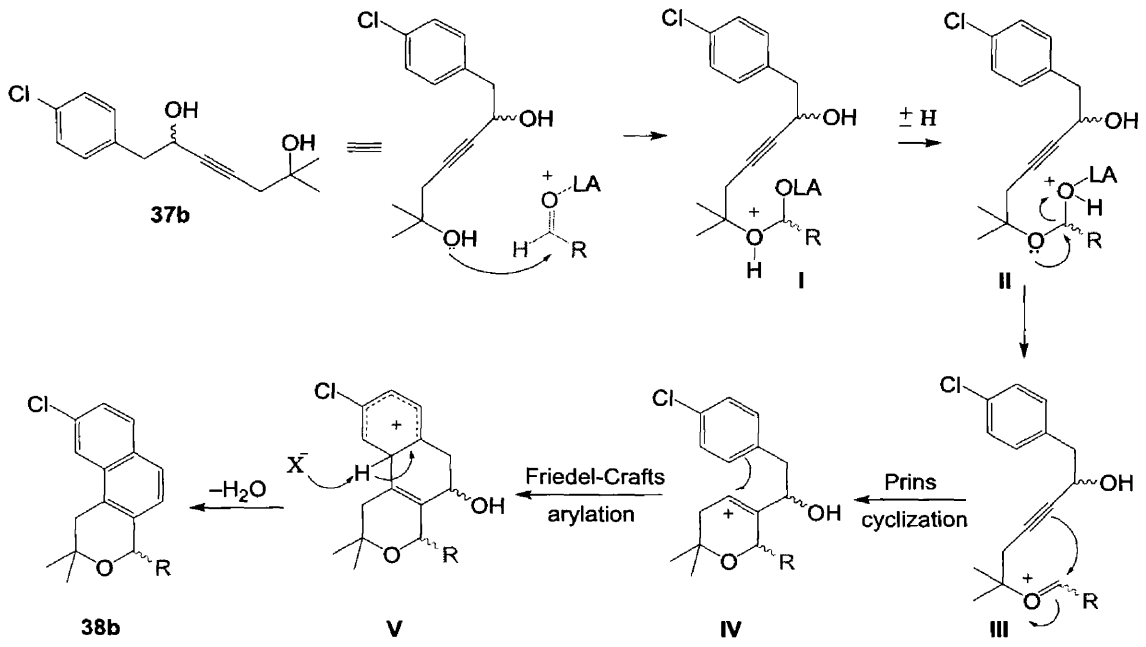



[a] Reagents and conditions: (a) DIBAL-H, THF, r.t., then $H_2O$, 75%; (b) 2-Iodoxybenzoic acid, MeCN, 80°C, 100% by $^1$H-NMR; or Dess-Martin periodinane reagent, $CHCl_3$, 0°C to r.t., 82-86%; or Dess-Martin periodinane reagent, DMF, 0°C to r.t., 77%; (c) TMS-acetylene, *n*-BuLi, THF, then $NH_4Cl$, -78°C to r.t., 71-88%; (d) $K_2CO_3$, THF, MeOH, $H_2O$, r.t., 74-98%; (e) *n*-BuLi, Isobutylene oxide, $BF_3$•$Et_2O$, THF, then $NH_4Cl$, -78°C, 30-51%; (f) Aldehyde, Lewis acid/Bronsted acid, $CH_2Cl_2$, -78°C to r.t., 15-89%.

The construction of the tricyclic benzo[*f*]isochromenes **38a**, **38b** and **38d** was started from alcohols **33a, 33b** and **33d**, respectively. Tricyclic benzo[*f*]isochromene **38c** was obtained from commercially available ester **32,** which was reduced with DIBAL-H to afford alcohol **33c** in 75% yield. All alcohols **33a-d**, upon treatment with oxidizing agents such as 2-Iodoxy-

benzoic acid (IBX) or Dess-Martin periodinane (DMP), generated the corresponding aldehydes **34a-d** in excellent yields. However, these aldehydes are not thermally stable and tend to decompose on silica gel during attempted purification by flash chromatography. Since oxidation of alcohols **33a-d** using IBX afforded aldehydes **34a-d**, which appeared pure by both TLC and $^1$H-NMR spectroscopy, the crude aldehydes were directly reacted with TMS-acetylide to afford TMS alkynols **35a-d** in good yields. Subsequent desilylation of **35a-d** using 3.0 equivalents of $K_2CO_3$ gave propargylic alcohols **36a-d** in excellent yield. The alkynediol precursors **37a-d** were synthesized from **36a-d** by treatment with *n*-BuLi to convert **36a-d** into dianions, which were then used to ring open isobutylene oxide in the presence of $BF_3 \cdot Et_2O$. Different aldehydes were then employed to react with alkynediols **37a-d** to afford tricyclic benzo[*f*]isochromenes **38a-d** as final products in moderate to high yields. The final reaction (conditions f), which includes three discrete chemical steps, is shown in **Scheme 2.2**.

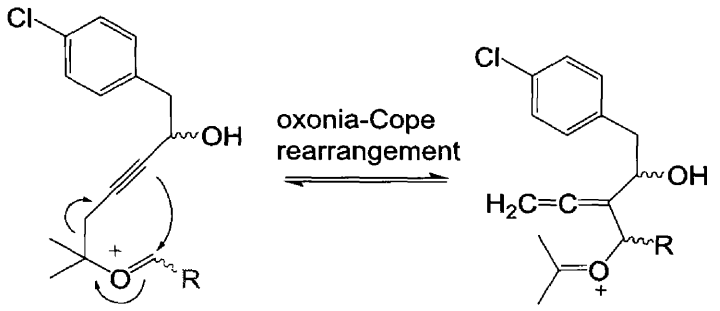
**Scheme 2.2.** Detailed steps of reaction f towards benzo[*f*]isochromene **38b**.




In alkynediol **37b**, the tertiary alcohol would attack the activated aldehyde to generate hemiacetal intermediate **I**, followed by proton transfer to produce another hemiacetal, **II**. Elimination then affords the oxocarbenium ion intermediate **III**, which is attacked by the tethered alkyne (alkynyl-Prins reaction) to generate the cationic dihydropyran intermediate **IV**. The resulting dihydropyranyl cation **IV** is then attacked by the pendant aryl ring to produce arenium ion intermediate **V** through Friedel-Crafts arylation. At last, the final benzo[*f*]isochromene **38b** was formed after dehydration and re-aromazation.

Studies revealed that oxonia-Cope rearrangement can be the main competitive reaction with the alkynyl-Prins cyclization.[31,27d,32] A proposed 2-oxonia-[3,3]-sigmatropic rearrangement from intermediate **III** is shown in eq 10, which would generate allenyl cation intermediate **VI**. The competition

between Prins cyclization and oxonia-Cope rearrangement is dependent on the relative stabilities of intermediates **III** and **VI**. As discussed on pages 14 of the introduction, several factors affecting alkynyl Prins cyclization were studied by Padron and coworkers,[27d,32]. In this thesis, experiments exploring electronic effects on the Friedel-Craft arylation and Prins cyclization were both conducted.



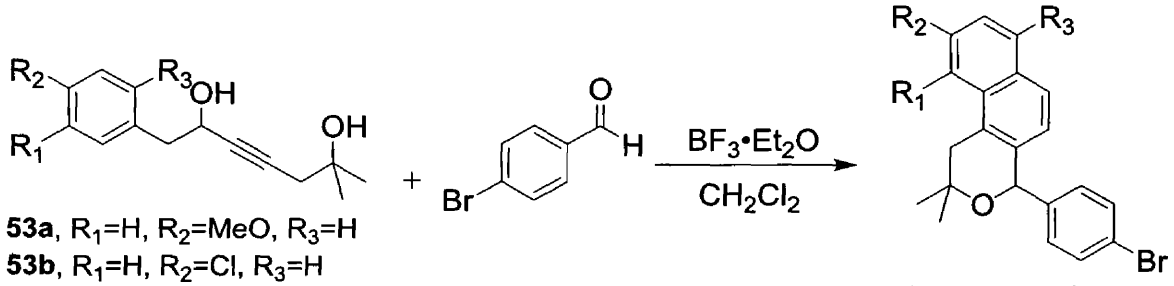

**III** **VI** (10)

## 2.2 OPTIMIZATION OF REACTIONS TOWARD ISOCHROMENES

### 2.2.1 RATIOS OF REACTION COMPONENTS

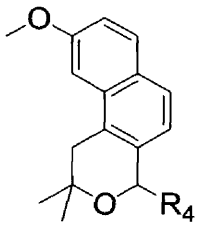
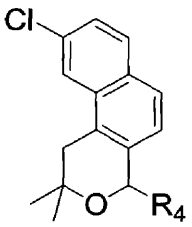
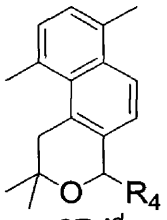
As a result of the previous paper,[30] 10 mol% excess of $BF_3$•$Et_2O$ and 20 mol% excess of aldehyde over alkynediol provided the best yields. However, when electron donating or withdrawing substituents were introduced into alkynediol precursor, the previous reaction conditions led to low yields (eq 9). In order to explore the optimal reaction protocol for each of the benzo[*f*]isochromenes, experiments using various equivalents of alkynediol, aldehyde and $BF_3$•$Et_2O$ were conducted, in which **37a**, **37b** and **37d** were used as starting alkynediols (**Table 1**).

**Table 1.** Different equivalents of alkynediol, aldehyde and acid activators.

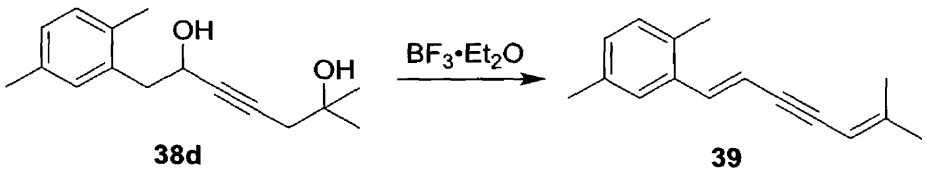



**53a**, $R_1$=H, $R_2$=MeO, $R_3$=H
**53b**, $R_1$=H, $R_2$=Cl, $R_3$=H
**53d**, $R_1$=Me, $R_2$=H, $R_3$=Me

**37a, 37b and 37d**

| Entry | Product | Alkynediol / aldehyde / $BF_3$•$Et_2O$ | Yield(%)[a] |
|---|---|---|---|
| 1 |  | 1.0 / 1.2 / 1.1 | 22 |
| 2 | | 1.0 / 1.2 / 2.0 | 26 |
| 3 | | 1.0 / 1.4 / 3.0 | 29 |
| 4 | | 1.0 / 2.0 / 5.0 | 23 |
| 5 | **37a**[b] | 1.0 / 1.2 / 3.0 | 22 |
| 6 |  | 1.0 / 1.2 / 1.1 | 24 |
| 7 | | 1.0 / 1.4 / 1.4 | 21 |
| 8 | | 1.0 / 1.4 / 3.0 | 61 |
| 9 | | 1.0 / 2.0 / 5.0 | 49 |
| 10 | **37b**[b,c] | 1.0 / 1.5 / 3.0 | 47 |
| 11 |  | 1.0 / 1.2 / 1.1 | 53 |
| 12 | | 1.0 / 1.2 / 2.0 | 49 |
| 13 | | 1.0 / 1.4 / 3.0 | 77 |
| 14 | **37d**[d] | 1.0 / 1.8 / 5.0 | 50 |

a. Yields are based on GC analysis using undecane as an internal standard.
b. Reactions were conducted under argon at 0.25 M in Alkynediol.
c. Selected results among 13 different reaction schemes.
d. Reactions were conducted under argon at 0.10 M in Alkynediol.




**38d** **39** (11)

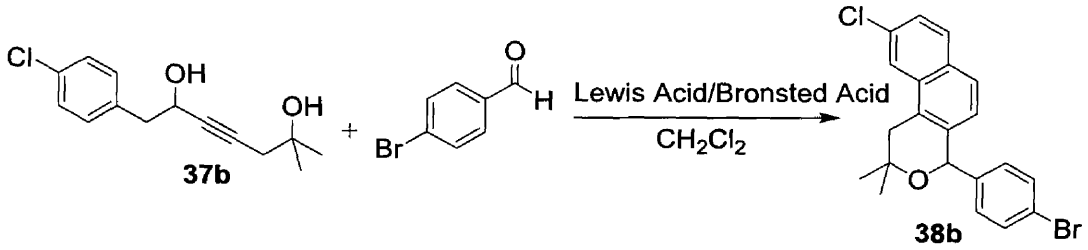
Generally, a large excess of Lewis acids can be used to activate aldehydes. However, too much of a Lewis acid can result in dehydration products of the alkynediol (eq 11) as well as aldol products from enolizeable aldehydes such as phenylpropionaldehyde (eq 12). Therefore, a compromise between aldehyde activation and side-reactions must be reached. For the reaction of alkynyediols **37a**, **37b** and **37d** with *p*-bromobenzaldehyde, the amount of excess $BF_3 \cdot Et_2O$ was substrate dependent. For all reactions in **Table 1**, the aromatic aldehyde *p*-bromobenzaldehyde was used so that no aldol product was possible.

In some cases, especially when 1.2 equivalents of aldehyde was used with **37a**, 2.0 equiv of $BF_3 \cdot Et_2O$ resulted in the best yield, but more than 2.0 equiv of Lewis acid tended to decrease the yield (see entries 2 and 5). When conducting the cascade reaction with **37d**, however, more than 1.1 equiv $BF_3 \cdot Et_2O$, led to lower yields (entries 11 and 12). A number of other factors such as the amount of alkynediol, aldehyde and acid activator, $pK_a$ of acid activator, temperature, reaction time, and type of solvent can also affect the competition between productive cascade reaction and degradation of starting material(s). In summary, 40 mol% excess of aldehyde and 200 mol% excess of $BF_3 \cdot Et_2O$ gave the highest yield for all of the alkynediols shown in **Table 1**.

## 2.2.2 CHOICE OF ACID ACTIVATOR

Several different Lewis and Brønsted acids were examined for reaction of alkynediol **37b** and *p*-bromobenzaldehyde towards **38b** (**Table 2**), as well as reaction of alkynediol **37d** and *p*-bromobenzaldehyde to form benzo[*f*]isochromene **38d** (**Table 3**).

**Table 2**. Brief survey of Lewis acid/Bronsted acid activators during reactions toward **38b.**




| Entry | Lewis Acid/Bronsted Acid | Yield(%)[a,b] |
|---|---|---|
| 1 | $BF_3 \cdot Et_2O$ | 61 |
| 2 | TfOH | 31 |
| 3 | TfOH[c] | 6 |
| 4 | pTSA | 14 |
| 5 | TMSOTf | 30 |
| 6 | TMSBr | 7 |
| 7 | $Cu(OTf)_2$ | 3 |

[a] Reactions were conducted under argon at 0.25 M in Alkynediol **37b** using 1.4 equiv. of aldehyde and 3.0 equiv. of corresponding Lewis acid/Bronsted acid unless specified.

[b] Yields are based on GC analysis using undecane as an internal standard.

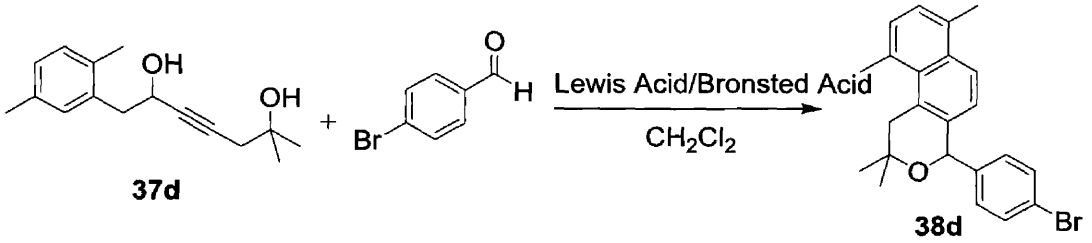
[c] Reaction was conducted using 0.5 equiv. of TfOH.

The chloride substituent in alkynediol **37b** is an *ortho/para*- director, and it has deactivating effect on the meta- position where the Friedel-Crafts arylation proceeds (**Scheme 2.2,** intermediate **IV**). According to **Table 1**, 1.4

equivalent of aldehyde and 3.0 equivalent of $BF_3 \cdot Et_2O$ (entry 8) gave the highest yield (61%). Therefore, the same ratio of aldehyde and different acid activators were applied toward **38b** (**Table 2**). Both stoichiometric (entry 2) and catalytic (entry 3) amounts of trifluoromethanesulfonic acid (TfOH) were used in the reaction. The stoichiometric amount of superacid TfOH gave relatively clean reaction mixtures after workup, but very moderate yields, whereas reaction using catalytic quantities of TfOH mostly resulted in recovered starting materials. When the weaker acid pTSA was used (entry 4), the reaction mixture showed multiples products by TLC analysis and only afforded the expected isochromene in 14% yield. The known Lewis acid TMSOTf (entry 5) was applied during the reaction cascade but also resulted in a moderate 30% yield. TMSBr (entry 6) was also employed to initiate the Prins cyclization, but only 7% yield was obtained. It is important to note that TMSBr provides a nucleophilic anion $Br^-$, which could attack the carbocation in dihydropyran intermediate **IV** in competition with the Friedel-Crafts arylation. The TLC of the reaction (entry 6) showed two obvious spots including isochromene product, but no pure brominated dihydropyran product was isolated or characterized. When using $Cu(OTf)_2$ (entry 7) as Lewis acid activator, only 3% yield was obtained. In summary, $BF_3 \cdot Et_2O$ (entry 8) gave the highest yield (61%) during this reaction cascade.

The dimethyl substituents in alkynediol **37d** have electron donating effect on the position where the Friedel-Crafts arylation proceeds (**Scheme 2.2,** intermediate **IV**). In **Table 3**, various Lewis and Brønsted acids were used to promote the reaction cascade. The catalytic amount of TfOH (entry 3) gave higher yield than a stoichiometric amount (entry 2), which means that

**Table 3**. Brief survey of Lewis acid/Bronsted acid activators in reactions toward **38d**.




| Entry | Lewis Acid/Bronsted Acid | Yield(%)[a,b] |
|---|---|---|
| 1 | $BF_3$•$Et_2O$ | 49 |
| 2 | TfOH | 27 |
| 3 | TfOH[c] | 31 |
| 4 | TFA[d] | trace |
| 5 | $In(OTf)_3$[e] | 19 |
| 6 | TMSOTf | 44 |
| 7 | $BF_2$•OTf•$Et_2O$ | 54 |
| 8 | HCl in $Et_2O$ | trace |
| 9 | $BF_3$•$Et_2O$, TMSBr[f] | 23 |

[a] Reactions were conducted under argon at 0.10 M in alkynediol **37d** using 1.2 equiv. of aldehyde and 2.0 equiv. of corresponding Lewis acid/Bronsted acid unless specified.

[b] Isolated yields after silica gel chromatography.

[c] Reaction was conducted using 0.1 equiv. of TfOH.

[d] Reaction was conducted using 10.0 equiv. of TFA.

[e] Reaction was conducted using 0.1 equiv. of $In(OTf)_3$.

[f] Reaction was conducted using 2.0 equiv. of $BF_3$•$Et_2O$ and 1.2 equiv. of TMSBr.

TfOH can serve as a catalyst to promote Prins cyclization. When adding TFA (entry 4) or HCl (entry 8) to the reaction, starting materials were mostly recovered and little expected product was observed according to GC analysis. In contrast, a catalytic amount of $In(OTf)_3$ (entry 5) afforded the expected product, but only in 19% yield.

Combinations of acids can also be effective. For instance, Aggarwal and coworkers[33] conducted research on a combination of $BF_3$•OEt and TMSOTf to afford a more powerful Lewis acid $BF_2$•OTf•$OEt_2$. Inspired by their research, $BF_3$•OEt and TMSOTf were combined in 1.0:1.0 ratio to form $BF_2$•OTf•$OEt_2$ (entry 7) to initiate the cascade sequence; the desired product was obtained in 54% yield. This combination Lewis acid provided higher yields than either $BF_3$•$OEt_2$ (entry 1) or TMSOTf alone (entry 6). Since no characterization methods were used to verify the structure of $BF_2$•OTf•$OEt_2$, it is, however, difficult to ensure formation of such a Lewis acid.

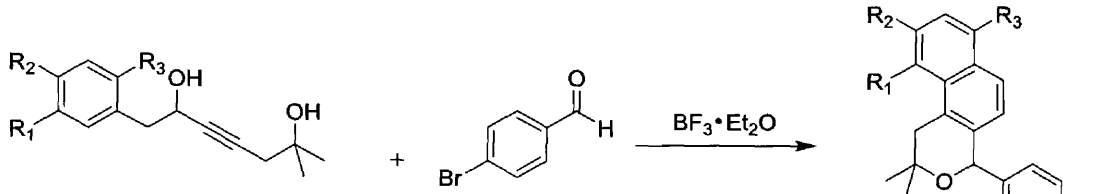
When the reaction sequence was initiated with 2.0 equiv. of $BF_3$•OEt and 1.2 equiv. of TMSBr (entry 9), a lower yield (23%) was observed compared to reaction using 2.0 equivalents of $BF_3$•$OEt_2$ (entry 1, 49% yield). The reduced yield could support the assumption that $Br^-$ attacks the cation in dihydropyran intermediate **IV** to afford a brominated dihydropyran instead of the desired isochromene that would result from Friedel-Crafts arylation (entry 6, **Table 2**). Due to factors including good yields, low cost, simple reaction

mixtures, and easy operational conditions, $BF_3 \cdot OEt_2$ was employed as the Lewis acid activator in remaining reactions described.

## 2.2.3 CHOICE OF SOLVENT

In order to determine the appropriate solvent for the reaction cascade towards benzo[*f*]isochromenes, aprotic solvents including $Et_2O$ and THF were also evaluated during reaction and the results are shown in **Table 4**.

**Table 4.** Brief survey of different solvents.




**37b**, $R_1$=H, $R_2$=Cl, $R_3$=H
**37d**, $R_1$=Me, $R_2$=H, $R_3$=Me

**38b** and **38d**

| Entry | Product | Solvent | Yield(%)[a] |
|---|---|---|---|
| 1 | **38b** | $CH_2Cl_2$[b] | 61[d] |
| 2 | **38b** | THF[b] | 16 |
| 3 | **38d** | $Et_2O$[c] | 36 |
| 4 | **38d** | $CH_2Cl_2$[c] | 49 |

a. Isolated yields after silica gel chromatography unless otherwise noted.
b. Reaction was conducted under argon at 0.25 M in Alkynediol **37b** using 1.4 equiv. of aldehyde and 3.0 equiv. of $BF_3 \cdot Et_2O$.
c. Reaction was conducted under argon at 0.10 M in Alkynediol **37d** using 1.2 equiv. of aldehyde and 2.0 equiv. of $BF_3 \cdot Et_2O$.
d. Yield is based on GC analysis using undecane as an internal standard.

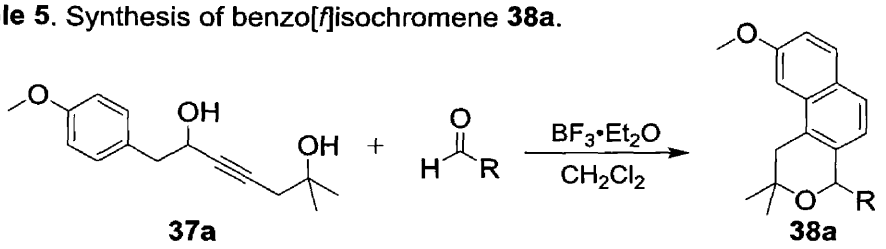
Although using THF (entry 1) and $Et_2O$ (entry 2) can effectively avoid the halogen exchange described in the introduction, use of these solvents

resulted in lower yield than reactions using $CH_2Cl_2$ as solvent. Based on the high yields and no evidence of halogen exchange in the reactions, $CH_2Cl_2$ was found to be the most appropriate solvent for the reaction cascade in this thesis.

## 2.3 EFFECTS OF SUBSTITUENTS IN ALKYNEDIOL

Alkynediols, including **37a-d,** were reacted with various aldehydes to afford different benzo[*f*]isochromenes. The results are shown in **Tables 5-8**.

**Table 5**. Synthesis of benzo[*f*]isochromene **38a**.



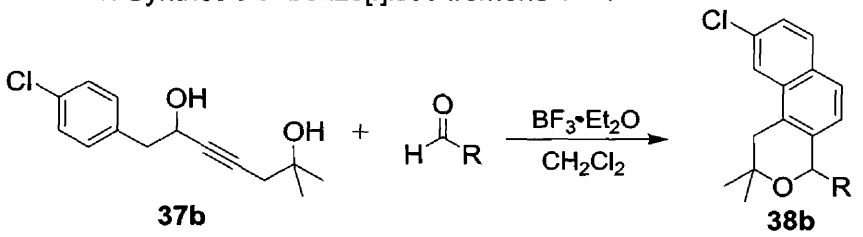

**37a** **38a**

| Entry | Product | Aldehyde (R) | Yield(%)[a,b] |
|---|---|---|---|
| 1 | **38a-1** | $PhCH_2CH_2$- | 15 |
| 2 | **38a-2** | *p*-$NO_2$-Ph- | 22 |
| 3 | **38a-3** | *p*-$CF_3$-Ph- | 25 |
| 4 | **38a-4** | *p*-Br-Ph- | 29 |

[a] Reactions were conducted under argon at 0.25 M in alkynediol **37a** using 1.4 equiv. of aldehyde and 3.0 equiv. of $BF_3$•$Et_2O$.

[b] Isolated yields after silica gel chromatography.

**Table 6**. Synthesis of benzo[*f*]isochromene **38b**.




**37b** **38b**

| Entry | Product | Aldehyde (R) | Yield(%)[a,b] |
|---|---|---|---|
| 1 | **38b-1** | Et- | 39 |
| 2 | **38b-2** | i-Pr- | 27 |
| 3 | **38b-3** | sec-Bu- | 36[c] |
| 4 | **38b-4** | $PhCH_2CH_2$- | 38 |
| 5 | **38b-5** | *p*-$NO_2$-Ph- | 45 |
| 6 | **38b-6** | *p*-$CF_3$-Ph- | 48 |
| 7 | **38b-7** | *p*-Br-Ph- | 61[d] |

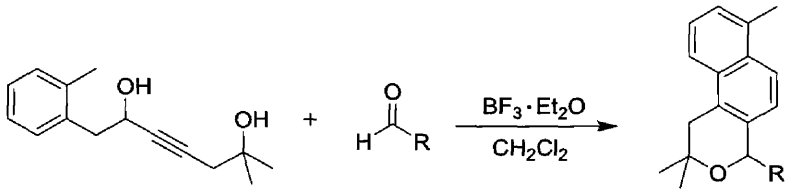
[a] Reactions were conducted under argon at 0.25 M in alkynediol **37b** using 1.4 equiv. of aldehyde and 3.0 equiv. of $BF_3$•$Et_2O$.

[b] Isolated yields after silica gel chromatography unless noted.

[c] A 2:1 mixture of diastereomers was obtained in a combined yield of 36%.

[d] Yield was obtained by GC analysis using undecane as internal standard.

**Table 7**. Synthesis of benzo[*f*]isochromene **38c**.



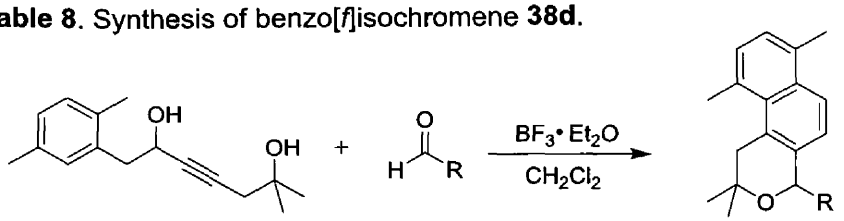

**37c** **38c**

| Entry | Product | Aldehyde (R) | Yield(%)[a,b] |
|---|---|---|---|
| 1 | **38c-1** | $PhCH_2CH_2$- | 57 |
| 2 | **38c-2** | *p*-$NO_2$-Ph- | 46 |
| 3 | **38c-3** | *p*-Br-Ph- | 62 |
| 4 | **38c-4** | *p*-$CH_3$-Ph- | 74 |

a. Reactions were conducted under argon at 0.10 M in alkynediol **37c** using 1.4 equiv. of aldehyde and 3.0 equiv. of $BF_3$• $Et_2O$.

b. Isolated yields after silica gel chromatography.

**Table 8**. Synthesis of benzo[*f*]isochromene **38d**.




**37d** **38d**

| Entry | Product | Aldehyde (R) | Yield(%)[a,b] |
|---|---|---|---|
| 1 | **38d-1** | $PhCH_2CH_2$- | 78 |
| 2 | **38d-2** | *p*-$NO_2$-Ph- | 53 |
| 3 | **38d-3** | *p*-Br-Ph- | 77 |
| 4 | **38d-4** | *p*-$CH_3$-Ph- | 89 |

a. Reactions were conducted under argon at 0.10 M in alkynediol **37d** using 1.4 equiv. of aldehyde and 3.0 equiv. of $BF_3 \cdot Et_2O$.
b. Isolated yields after silica gel chromatography.

Both aliphatic and aromatic aldehydes were reacted with different alkynediols to furnish various benzo[*f*]isochromenes. Phenylpropionaldehyde is an aliphatic aldehyde, which was used to react with each of the four alkynediols. As a result, when substituents in the alkynediol have more electron donating effect on the position where the Friedel-Crafts arylation proceeds (**Scheme 2.2,** intermediate **IV**), more expected benzo[*f*]-isochromene products were generated (entry 1 in **Table 5** has 15% yield, entry 4 in **Table 6** has 38% yield, entry 1 in **Table 7** has 57% yield and entry 1 in **Table 8** has 78% yield). For aromatic aldehydes (e.g. *p*-nitrobenz-aldehyde and *p*-bromobenzaldehyde), the benzo[*f*]isochromene yields were higher when substituents in the alkynediol have more electron donating effect on the position where the Friedel-Crafts arylation proceeds (**Scheme 2.2,**

intermediate **IV**). The same results were obtained when using other aldehydes listed in **Table5-8**.

This is likely because the Friedel-Craft arylation is more efficient when a more electron-rich aryl moiety attacks dihydropyranyl intermediate **IV**. Moreover, electron donating groups in alkynediol **37** (e.g., $CH_3$) can better stabilize the cation dihydropyran intermediate **IV,** resulting in decreasing the possibility of oxonia-Cope rearrangement to allenic structure **VI** (eq 10). In summary, more electron rich substituents in the alkynediol can effectively increase the yield.

## 2.4 EFFECTS OF DIFFERENT ALDEHYDES

As the results in **Table 6** show, when R becomes more electron-rich, more desired benzo[*f*]isochromene products was isolated. Similar results are shown in **Tables 5**, **7** and **8**.

As previously discussed, Padron showed that the oxonia-[3,3]-sigmatropic rearrangement can be competitive with Prins cyclization. The relative stabilities of oxocarbenium ion intermediate **III** and allenyl cation intermediate **VI** are crucial to determine which of the two pathways is more favorable. Padron and coworkers[27d,32] found that TMS group can lead to a less-favored oxonia-Cope rearrangement (**Figure 2.1**).

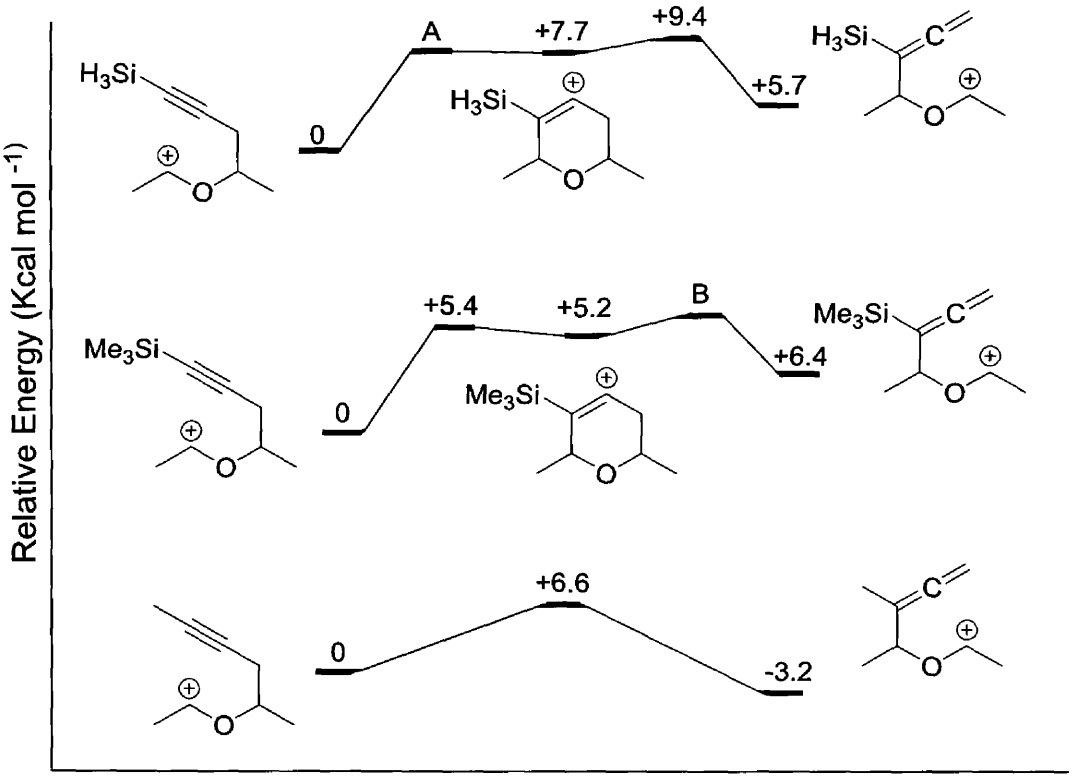
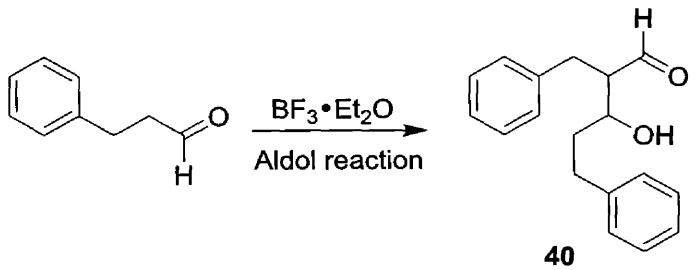



**Figure 2.1**. Silyl substituent effects on the relative-energy profile of oxonia-Cope rearrangement[27d,35]

Although the energy gap between oxocarbenium ion intermediate **III** and allenyl cation intermediate **VI** has not been calculated, results from **Tables 5-8** reveal that more electron-rich aldehydes result in higher yields of benzo[*f*]isochromenes. For example, in **Table 8**, yields increase from 53% to 89% (entry 2 to entry 4) as the aldehydes become more electron donating. That result is because electron rich aldehydes can better stabilize the oxocarbenium ion intermediate **III** (**Scheme 2.2**) by donating electrons to the carbon in O=C bond. Also **Tables 5-8** reveal that most aryl 2,4-dihydro-*1H*-benzo[*f*]isochromenes were isolated in higher yield than alkyl 2,4-dihydro-*1H*-

benzo[*f*]isochromenes. For example, in **Table 6**, alkyl isochromenes (entries 1-4) were only isolated in 27% to 39% yields, whereas the aryl substituted isochromenes were obtained in 45% to 61% yields (entries 5-7). The reasons can be summarized as follows. First, alkyl 2,4-dihydro-*1H*-benzo[*f*]isochromenes (e.g., **38b-4**, **38c-1** and **38d-1**) are easily oxidized to lactones as described by Hinkle and Lewis.[30] Although the lactone structures were not observed for the alkyl 2,4-dihydro-*1H*-benzo[*f*]isochromenes in the current work, there are other side products formed during the cascade that were not isolated. Secondly, the oxocarbenium ion intermediate **III** (**Scheme 2.2**) can be better stabilized by an aromatic substituent that is conjugated with the O=C bond. Thirdly, aldol product **40** from enolizeable phenylpropionaldehyde was isolated (eq 12), and aldol reactions with enolizeable aldehydes would decrease the yields of alkyl 2,4-dihydro-*1H*-benzo[*f*]isochromenes.




**40** (12)

**Tables 7** and **8** do not show a significant difference between alkyl 2,4-dihydro-*1H*-benzo[*f*]isochromenes and phenyl 2,4-dihydro-*1H*-benzo[*f*]isochromenes. It is possible that the mono-methyl or di-methyl groups in alkynediol can better stabilize intermediate **V** (**Scheme 2.2**) as discussed

above in section 2.3. As a result, the Prins cyclization is more favorable and fewer side products would be generated. Therefore, when comparing phenylpropionaldehyde and *p*-nitrobenzaldehyde, the more electron-rich aldehyde can stabilize the initial oxocarbenium ion, **III** and reduce the propensity for oxonia-Cope rearrangements.

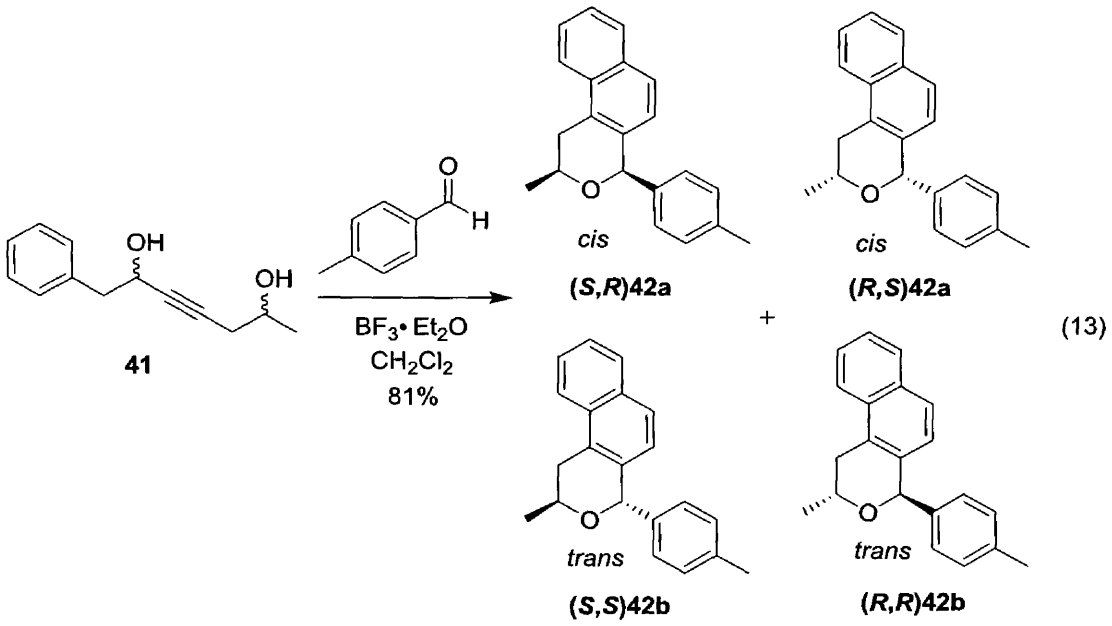
As unpublished research by Professor Andrew Harned at the University of Minnesota has revealed, the Prins cyclization/Friedel-Crafts arylation may well be concerted reactions in which no intermediate such as **IV** is involved. When using strongly electron-withdrawing *p*-nitrobenzaldehyde during the cascade sequence (entry 2 in **Table 5**, entry 5 in **Table 6**, entry 2 in **Table 7** and entry 2 in **Table 8**), the oxocarbenium ion intermediate **III** (eq 10) would be destabilized by the electron-withdrawing nitro group whereas an oxocarbenium ion (e.g., **VI** in eq 10) resulting from oxonia-Cope rearrangement would be stabilized. However, methyl substituted isochromenes (**38d-2** and **38c-2**) were isolated in higher yields than chloride or methoxy substituted isochromenes (**38b-5** and **38a-2**); these results support the idea that the alkynyl-Prins and Friedel-Crafts reactions are concerted.

## 2.5 SYNTHESIS OF ISOCHROMENES WITH TWO CHIRAL CENTERS

In order to further study the stereoselectivity of this reaction cascade, both racemic and chiral versions of 1-phenylhept-3-yne-2,6-diol (**41** and **43**,

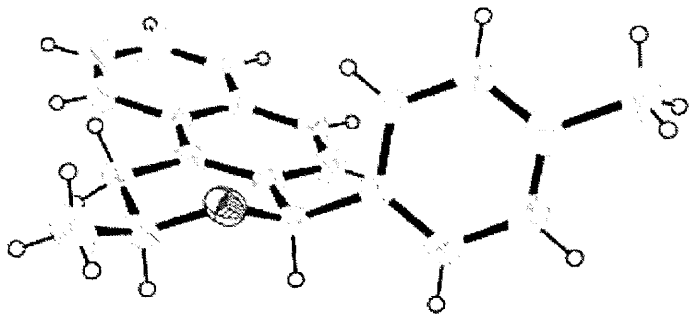
respectively) and *p*-tolualdehyde were employed to generate isochromenes with two chiral centers.

At first, the racemic version of 1-phenylhept-3-yne-2,6-diol **41** was used (eq 13) and afforded 2-methyl-4-(*p*-tolyl)-1,4-dihydro-2*H*-benzo[*f*]-isochromenes **42a** and **42b** in 81% combined yield.



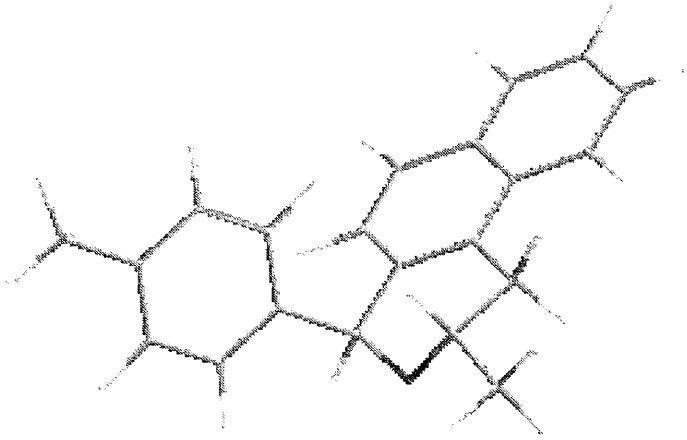

(13)

Interestingly, both *cis*- (**42a**) and *trans*- (**42b**) fused tricyclic products were obtained, and there was a slight preference for the *cis*- diastereomer (*cis:trans* = 1.3:1.0). After separation of the diastereomers by column chromatography, the structure of the *cis*-fused diastereomer (**42a**) was confirmed by X-ray crystallographic analysis (**Figure 2.2**), whereas the structure of *trans*- fused diastereomer (**42b**) was confirmed by $^{1}$H-NMR, $^{13}$C-APT, $^{13}$C-DEPT, g- COSY, HSQCAD, NOESY1D analyses and high-resolution mass spectrometry (**Figure 2.3**).



**(*S*,*R*)42a** and **(*R*,*S*)42a**

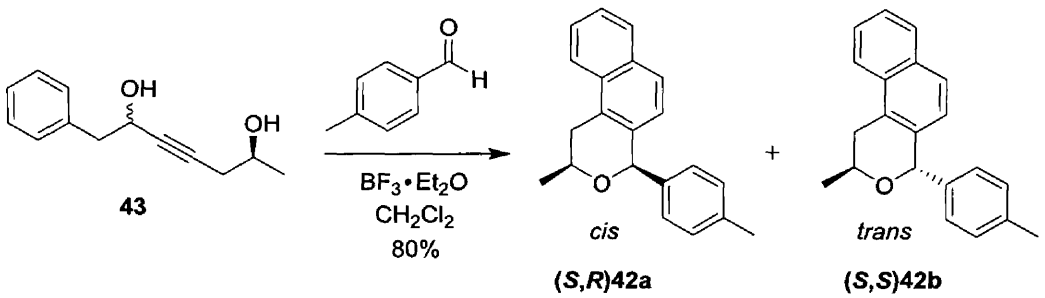
**Figure 2.2** Crystal structure of *cis*- fused diastereomer.



**(*S*,*S*)42b** and **(*R*,*R*)42b**

**Figure 2.3.** Structure of *trans*- fused diastereomer.

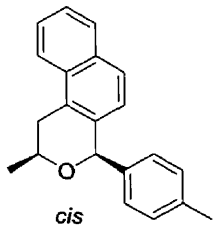
(*6S*)-1-Phenylhept-3-yne-2,6-diol **43**, which was synthesized from enantiomerically-pure (*S*)-propylene oxide, was then reacted with *p*-tolualdehyde to furnish *cis*- and *trans*-benzo[*f*]isochromenes (eq 14). This reaction proceeded in 80% combined yield and resulted in a 1.4:1.0 ratio ($^1$H NMR) of *cis*- and *trans*- fused diastereomers.



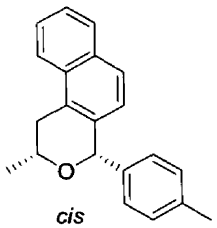

(14)

In order to investigate whether each product from eq. 14 is enantiomerically-pure, HPLC analyses were performed using a chiral AD-H column. As shown in **Table 9**, both entry 1 and entry 2 exhibited 1.0:1.0 ratio of each enantiomer, which indicates that when using racemic alkynediol **41** in the reaction cascade, enantiomers in each pair of diastereomers are in 1.0:1.0 ratio. Therefore, the yields of *cis*- products **(*S*,*R*)42a** and **(*R*,*S*)42a** are both 23%, and the yields of *trans*- products **(*S*,*S*)42b** and **(*R*,*R*)42b** are both 17.5%. Entry 3 and entry 4 were, however, synthesized from chiral alkynediol **43**, and both *cis*- and *trans*- fused diastereomers were isolated as single enantiomer according to **Table 9**. This means the reaction sequence (eq 14) can completely retain the defined stereocenter from alkynediol **43**.

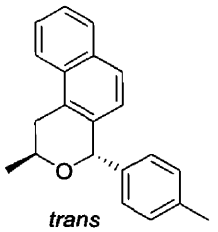
**Table 9.** HPLC analysis of benzo[*f*]isochromenes with two chiral centers



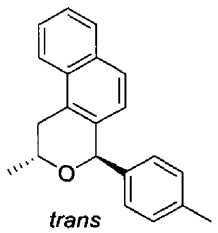
*cis*
**42a**



*cis*
**42b**



*trans*
**42c**



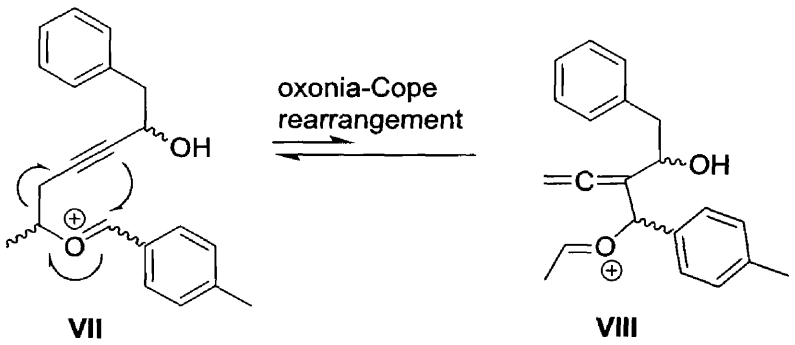
*trans*
**42d**

| Entry | 1[a] | 2[b] | 3[c] | 4[d] |
|---|---|---|---|---|
| Sample | **42a 42b** | **42c 42d** | **42a** | **42c** |
| Retention time (min) | 4.225 4.524 | 6.069 6.395 | 4.190 | 6.064 |

HPLC image

a. Samples from entry 1 are the *cis* products collected in reaction **41** to **42** (eq 13).
b. Samples from entry 2 are the *trans* products collected in reaction **41** to **42** (eq 13).
c. Samples from entry 3 are the *cis* product collected in reaction **43** to **42** (eq 14).
d. Samples from entry 4 are the *trans* product collected in reaction **43** to **42** (eq 14).

Both reactions involving racemic and chiral versions of 1-phenylhept-3-yne-2,6-diol and *p*-tolualdehyde (eq 13 and 14) afforded benzo[*f*]isochromenes in high yields. There are two reasons that explain the high yields. Firstly, the aromatic moiety from *p*-tolualdehyde can form a conjugation system with O=C bond in oxocarbenium ion intermediate **VII** (eq 15), which can better stabilize **VII**. Secondly, the methyl substituent in *p*-tolualdehyde can *further* help stabilize oxocarbenium ion intermediate **VII** by donating electrons into the carbon of the O=C bond; the oxonia-Cope rearrangement would therefore be less favored.




(15)

## 2.6 CONCLUSIONS

In summary, research has been conducted on a two-component, four-reaction cascade to rapidly form novel tricyclic molecules (reaction f, **Scheme 2.1**). The reaction cascade proceeds with various alkynediol substrates and aldehydes, and provides an efficient synthetic strategy to assemble tricyclic isochromenes in a single reaction vessel. Optimization studies revealed that 1.0 equiv. of alkynediol, 1.4 equiv. of aldehyde and 3.0 equiv. of $BF_3{\cdot}Et_2O$ in $CH_2Cl_2$ gave less complex reaction mixtures and afforded benzo[*f*]isochromene products in highest yields.

In order to investigate factors affecting alkynyl-Prins cyclization and a possible 2-oxonia-[3,3]-rearrangement, both aliphatic and aromatic aldehydes were reacted with each of four alkynediols (reaction f, **Scheme 2.1, 37a-d**). As the substituent groups ($R_1$, $R_2$ and $R_3$) in the alkynediol become more electron rich, the Friedel-Crafts arylation became more efficient and the cascade afforded more desired benzo[*f*]isochromene products. Stabilizing the oxocarbenium ion intermediates can help disfavor the oxonia-Cope

rearrangement. As the electron density of $R_4$ increases, the reaction cascade favors the Prins cyclization products instead of isomers resulting from sigmatropic rearrangement. Some side products from the reaction cascade were isolated which include dehydration products of alkynediol and aldol products from phenylpropionaldehyde.

Finally, the stereoselectivity of this reaction cascade was examined using racemic and chiral versions of 1-phenylhept-3-yne-2,6-diol and *p*-tolualdehyde to generate isochromenes with two chiral centers. Although both *cis*- and *trans*-fused tricyclic products were obtained, there was a slight preference for the *cis*- diastereomer (*cis:trans* = 1.3:1.0 to 1.4:1.0). When using alkynediol with a defined chiral center, both *cis*- and *trans*- fused diastereomers were isolated as single enantiomer. Investigations on the variations of the reaction cascade and more synthetic applications will be further studied.

# CHAPTER 3. EXPERIMENTAL

## 3.1 GENERAL INFORMATION

All reactions were carried out under argon gas unless otherwise noted. Dichloromethane was distilled from $CaH_2$; THF was purified by a Solv-Tek® alumina drying column. Flash column chromatography was performed using Sorbent Technologies 40-75μm silica gel (200x400 mesh). Thin layer chromatography was conducted using Sorbent Technologies general-purpose silica gel HL TLC plates on glass. Visualization was accomplished with UV light or by heating plates dipped in Cerium Ammonium Molybdate or potassium permanganate solutions. Fourier transform infrared (FT-IR) spectroscopy was recorded using a DIGILAB FTS 7000 series FTIR spectrophotometer. Single crystal determinations were carried out with a Bruker *SMART Apex II* diffractometer using graphite-monochromated Cu $K_\alpha$ radiation. $^1H$ NMR spectra were recorded on Varian Mercury FTNMR (400 MHz) or Agilent Vnmr J4.1 (400 MHz) spectrometers and are reported in ppm using solvent as an internal standard (tetramethylsilane at 0.00 ppm). Proton-decoupled $^{13}C$-NMR spectra were recorded on Varian Mercury FTNMR (400 MHz) or Agilent Vnmr J4.1 (400 MHz) spectrometers and are reported in ppm using solvent as an internal standard ($CDCl_3$ at 77.23 ppm). Quaternary carbons (C) are listed as (q), methine carbons (CH) are listed as (t), methylene carbons ($CH_2$) are listed as (s), and methyl carbons ($CH_3$) are listed as (p). Nuclear Overhauser Effects (NOEs) and two-dimensional NMR

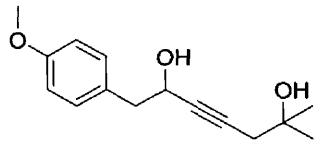
spectra, including gCOSY and HSQCAD, were recorded on an Agilent Vnmr J4.1 spectrometer. Gas chromatographic (GC) analyses were conducted using a Varian 3900 spectrometer equipped with an FID. Gas chromatography–mass spectrometry (GC-MS) analyses were performed using an Agilent Technologies 5973 network mass selective detector and 6890N network GC system. High-performance liquid chromatography (HPLC) was performed using SHIMADZU UFLC with the following components: DGU-20A 5R degassing unit, LC-20AT liquid chromatograph, SIL-20AC HT auto sampler, CBM-20A communications bus module, SPD-M20A diode array detector and CTO-20A column oven. The type of chiral column used in HPLC analysis was an AD-H (4.6mm$\Phi$x250mml, particle size 5μm) from CHIRALPAK. High Resolution Mass Spectrometry (HRMS) analyses were completed by the Cosmic Service Center at Old Dominion University through positive electrospray ionization on a Bruker 12 Tesla APEX –Qe FTICR-MS with and Apollo II ion source.

## 3.2 SYNTHESIS OF ALKYNEDIOL

**General Procedure A for Alkynediol Synthesis. Synthesis of 1-(2,5-dimethylphenyl)-6-methylhept-3-yne-2,6-diol (37d):** To a three-neck round bottom flask was added alkyne mono-alcohol **36d** (3.0483g, 17.49mmol, 1.0 equiv) in dry THF under argon gas, followed by *n*-BuLi (2.2 M, 17.49ml, 38.49mmol, 2.2 equiv) dropwise at -78°C. After 1hour, $BF_3$•$Et_2O$ (3.7296g,

26.24mmol, 1.5 equiv) was added at -78°C and stirred for 15 min. Then isobutylene oxide (1.5594g, 20.99mmol, 1.2 equiv) was added dropwise, and the solution stirred for additional 1 h under argon at -78°C. The mixture was then warmed to rt, quenched with saturated $NH_4Cl$ and extracted with $Et_2O$ or EtOAc. The organic layers were combined, washed with Brine, dried over $MgSO_4$, and concentrated in vacuo. The crude product was then purified by flush column chromatography using 40-60% hexanes in ethyl acetate, and obtained 1.6308g product in 38% yield.

**1-(4-methoxyphenyl)-6-methylhept-3-yne-2,6-diol (37a):**

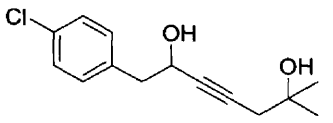



Chemical Formula: $C_{15}H_{20}O_3$
Exact Mass: 248.14
Molecular Weight: 248.32
m/z: 248.14 (100.0%), 249.14 (16.2%), 250.15 (1.9%)
Elemental Analysis: C, 72.55; H, 8.12; O, 19.33

The compound was prepared using General Procedure A and purified by flash column chromatography using 40-60% hexanes in ethyl acetate to afford 40% average yields as a viscous yellow oil. $R_f$ = 0.26 (60% hexanes in ethyl acetate). IR (neat): 3414 (broad), 3038, 2981, 2941, 2886, 2843, 2213, 1671, 1615, 1516, 1302, 1249, 1180, 1035, 906, 821 $cm^{-1}$. $^1H$ NMR (400 MHz, $CDCl_3$): δ = 7.17 (d, *J* = 8.6Hz, 2H), 6.83 (d, *J* = 8.2Hz, 2H), 4.49 (s, 1H), 3.75 (s, 4H), 2.95-2.86 (m, 3H), 2.32 (d, *J* = 1.6Hz, 2H), 1.23 (s, 6H). $^{13}C$ NMR (100 MHz, $CDCl_3$): δ = 158.38 (q), 130.74 (t), 129.24 (q), 113.76 (t), 83.62 (q), 82.72 (q),

70.13 (q), 63.42 (t), 55.26 (p), 43.46 (s), 34.20 (s), 28.65 (p), 28.58 (p). HRMS (CI): *m/z* $[M+Na]^+$ calcd for $C_{15}H_{20}O_3Na$: 271.1305; found: 271.1307.

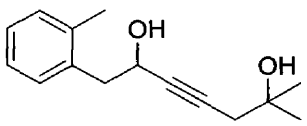
**1-(4-chlorophenyl)-6-methylhept-3-yne-2,6-diol (37b):**




Chemical Formula: $C_{14}H_{17}ClO_2$
Exact Mass: 252.09
Molecular Weight: 252.74
m/z: 252.09 (100.0%), 254.09 (32.0%), 253.10 (15.4%), 255.09 (4.9%), 254.10 (1.5%)
Elemental Analysis: C, 66.53; H, 6.78; Cl, 14.03; O, 12.66

The title compound was prepared according to General Procedure A and purified by flash column chromatography using 40-60% hexanes in ethyl acetate to afford 35% average yields as a viscous yellow oil. $R_f$ = 0.16 (60% hexanes in ethyl acetate). IR (neat): 3357 (broad), 3056, 2974, 2933, 2879, 2281, 2230, 1896, 1653, 1599, 1493, 1410, 1381, 1265, 1152, 1090, 1037, 905, 808, 739 $cm^{-1}$. $^1H$ NMR (400 MHz, $CDCl_3$): δ = 7.26-7.17 (m, 4H), 4.51 (s, 1H), 3.72 (broad s, 1H), 2.93-2.90 (m, 2H), 2.78 (broad s, 1H), 2.31 (d, *J* = 2.0Hz, 2H), 1.22 (s, 6H). $^{13}C$ NMR (100 MHz, $CDCl_3$): δ = 135.69 (q), 132.66 (q), 131.30 (t), 131.23 (t), 128.49 (t), 128.38 (t), 83.36 (q), 83.17 (q), 70.30 (t), 63.08 (t), 43.61 (s), 34.21 (s), 28.77 (p), 28.68 (p). HRMS (CI): *m/z* $[M+Na]^+$ calcd for $C_{14}H_{17}ClO_2Na$: 275.0809; found: 275.0813.

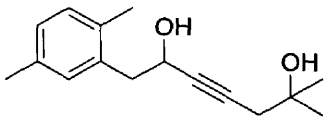
**6-methyl-1-(o-tolyl)hept-3-yne-2,6-diol (37c):**




Chemical Formula: $C_{15}H_{20}O_2$
Exact Mass: 232.15
Molecular Weight: 232.32
m/z: 232.15 (100.0%), 233.15 (16.5%), 234.15 (1.7%)
Elemental Analysis: C, 77.55; H, 8.68; O, 13.77

This diol was prepared according to General Procedure A and was purified by flash column chromatography using 40-60% hexanes in ethyl acetate to afford 30% yield as a viscous yellow oil. $R_f$ = 0.24 (60% hexanes in ethyl acetate), or $R_f$ = 0.38 (40% hexanes in ethyl acetate). IR (neat): 3357 (broad), 3065, 3026, 2980, 2931, 2288, 2230, 1495, 1463, 1383, 1156, 1032, 906, 745 $cm^{-1}$. $^1H$ NMR (400 MHz, $CDCl_3$): δ = 7.23-7.20 (m, 1H), 7.16-7.12 (m, 3H), 4.60 (t, *J* = 6.8Hz, 1H), 3.34 (broad s, 1H), 3.07 (dd, *J* = 13.7, 7.0Hz, 1H), 3.00 (dd, *J* = 13.7, 7.0Hz, 1H), 2.58 (broad s, 1H), 2.37 (s, 3H), 2.35 (d, *J* = 1.9Hz, 2H), 1.25 (s, 6H). $^{13}C$ NMR (100 MHz, $CDCl_3$): δ = 136.97 (q), 135.51 (q), 130.61 (t), 130.54 (t), 127.08 (t), 126.03 (t), 83.80 (q), 82.69 (q), 70.13 (q), 62.76 (t), 41.57 (s), 34.42 (s), 28.78 (p), 28.75 (p), 19.88 (p). HRMS (CI): *m/z* $[M+Ma]^+$ calcd for $C_{15}H_{20}O_2Na$: 255.1356; found: 255.1358.

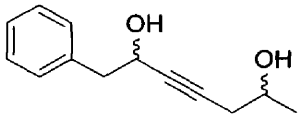
**1-(2,5-dimethylphenyl)-6-methylhept-3-yne-2,6-diol (37d):**




Chemical Formula: $C_{16}H_{22}O_2$
Exact Mass: 246.16
Molecular Weight: 246.35
m/z: 246.16 (100.0%), 247.17 (17.6%), 248.17 (1.9%)
Elemental Analysis: C, 78.01; H, 9.00; O, 12.99

This compound was synthesized according to General Procedure A and purified by flash column chromatography using 40-60% hexanes in ethyl acetate to afford average yields of 36% as a viscous yellow oil. $R_f$ = 0.26 (60% hexanes in ethyl acetate), or $R_f$ = 0.45 (40% hexanes in ethyl acetate). IR (neat): 3391, 2979, 2933, 2872, 2733, 2233, 1618, 1505, 1460, 1381, 1158, 1036, 906, 809 $cm^{-1}$. $^1H$ NMR (400 MHz, $CDCl_3$): δ = 7.02-6.91 (m, 3H), 4.54 (t, *J* = 6.4Hz, 1H), 3.15 (s, 1H), 2.98 (dd, *J* = 13.7, 7.0Hz, 1H), 2.92 (dd, *J* = 13.7, 7.0Hz, 1H), 2.51 (s, 1H), 2.31 (s, 2H), 2.28 (s, 3H), 2.26 (s, 3H), 1.21 (s, 6H). $^{13}C$ NMR (100 MHz, $CDCl_3$): δ = 135.35 (q), 135.29 (q), 133.74 (q), 131.36 (t), 130.40 (t), 127.71 (t), 83.82 (q), 82.56 (q), 70.12 (q), 62.73 (t), 41.59 (s), 34.38 (s), 28.74 (p), 28.70 (p), 21.07 (p), 19.37 (p). HRMS (CI): *m/z* $[M+Na]^+$ calcd for $C_{16}H_{22}O_2Na$: 269.1512; found: 269.1514.

**1-phenylhept-3-yne-2,6-diol (41):**

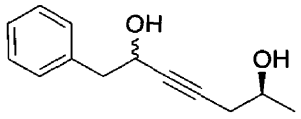



Chemical Formula: $C_{13}H_{16}O_2$
Exact Mass: 204.12
Molecular Weight: 204.27
m/z: 204.12 (100.0%), 205.12 (14.3%), 206.12 (1.4%)
Elemental Analysis: C, 76.44; H, 7.90; O, 15.66

The compound was prepared by General Procedure A from propargylic alcohol and racemic propylene oxide. The crude diol

was purified by flash column chromatography using 40-60% hexanes in ethyl acetate to afford 67% yield[34] as a viscous yellow oil. $R_f$ = 0.28 (50% hexanes in ethyl acetate). IR (neat): 3379 (broad), 3091, 3068, 3031, 2973, 2930, 2874, 2234, 1455, 1341, 1094, 1040, 940, 741, 700 $cm^{-1}$. $^1H$ NMR (400 MHz, $CDCl_3$): δ = 7.14-7.03 (m, 5H), 4.39-4.34 (m, 1H), 3.72-3.64 (m, 1H), 2.78 (overlapping d, *J* = 6.4Hz, 2H), 2.80 (broad s, 2H), 2.18 (unresolved dd of m, *J* = 16.7, 4.7Hz, 1H), 2.08 (APP ddq, *J* = 16.6, 6.7, 0.9Hz, 1H), 1.02 (d, *J* = 6.2Hz, 3H). $^{13}C$ NMR (100 MHz, $CDCl_3$): δ = 137.12 (q), 129.89 (t), 128.50 (t), 126.96 (t), 83.20 (q), 83.18 (q), 82.91 (q), 82.88 (q), 66.44 (t), 66.39 (t), 63.43 (t), 63.40 (t), 44.45 (s), 44.43 (s), 29.30 (s), 29.28 (s), 22.39 (p), 22.37 (p). HRMS (CI): *m/z* $[M+Na]^+$ calcd for $C_{13}H_{16}O_2Na$: 227.1043; found: 227.1045.

**(*6S*)-1-phenylhept-3-yne-2,6-diol (43):**




Chemical Formula: $C_{13}H_{16}O_2$
Exact Mass: 204.12
Molecular Weight: 204.27
m/z: 204.12 (100.0%), 205.12 (14.3%), 206.12 (1.4%)
Elemental Analysis: C, 76.44; H, 7.90; O, 15.66

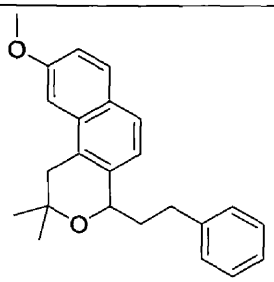
The compound was prepared in the same manner as **41** but with *S*-propylene oxide. The crude diol was purified by flash column chromatography using 40-60% hexanes in ethyl acetate to afford 44% yield as a viscous yellow oil. $R_f$ = 0.27 (50% hexanes in ethyl acetate). IR (neat): 3379 (broad), 3091, 3068, 3031, 2973, 2930, 2874, 2234, 1455, 1341, 1094, 1040, 940, 741, 700 $cm^{-1}$. $^1H$ NMR (400 MHz, $CDCl_3$): δ = 7.32-7.21 (m, 5H), 4.57-4.52 (m, 1H), 3.91-

3.82 (m, 1H), 3.26 (broad s, 1H), 2.96 (overlapping d, $J$ = 6.6Hz, 2H), 2.81 (broad s, 1H), 2.37 (dddd, $J$ = 16.6, 4.7, 1.9, 0.8Hz, 1H), 2.26 (dddd, $J$ = 16.6, 7.2, 1.9, 0.8Hz, 1H), 1.18 (d, $J$ = 6.3Hz, 3H). $^{13}C$ NMR (100 MHz, $CDCl_3$): δ = 137.14 (q), 129.86 (t), 128.47 (t), 126.92 (t), 83.18 (q), 83.16 (q), 82.89 (q), 82.87 (q), 66.43 (t), 66.37 (t), 63.40 (t), 63.37 (t), 44.42 (s), 29.26 (s), 29.24 (s), 22.37 (p), 22.35 (p). HRMS (CI): *m/z* $[M+Na]^+$ calcd for $C_{13}H_{16}O_2Na$: 227.1043; found: 227.1045.

## 3.3 SYNTHESIS OF ISOCHROMENES

**General Procedure B for Synthesis of Benzo[*f*]isochromenes. Synthesis of 2,2,7,10-tetramethyl-4-(p-tolyl)-1,4-dihydro-*2H*-benzo[*f*]isochromene (38d-4):** To a round bottom flask was added *p*-tolualdehyde (0.0477g, 0.40mmol, 1.4 equiv) in dry $CH_2Cl_2$ under argon gas at -78°C, followed by $BF_3 \cdot Et_2O$ (0.1210g, 0.85mmol, 3.0 equiv) dropwise. Then alkynediol **37d** (0.0700g, 0.28mmol, 1.0 equiv, 0.10 M) in $CH_2Cl_2$ was added dropwise at -78°C. The mixture was then warmed to room temperature and stirred under argon gas. After 6-12 hours the reaction was quenched with saturated $NaHCO_3$ and extracted with $Et_2O$ or EtOAc. The combined organic layers were washed with brine and $NaHSO_3$, dried over $MgSO_4$ and then concentrated in vacuo. The crude product was purified by flash column chromatography using 0-80% hexanes in dichloromethane, and obtained product in 89% yield.

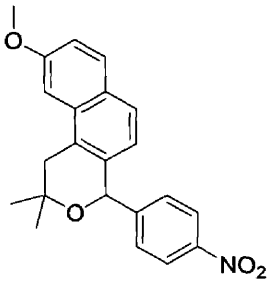
**9-methoxy-2,2-dimethyl-4-phenethyl-1,4-dihydro-2H-benzo[f]iso-chromene (38a-1):**



Chemical Formula: $C_{24}H_{26}O_2$
Exact Mass: 346.19
Molecular Weight: 346.47
m/z: 346.19 (100.0%), 347.20 (26.3%), 348.20 (3.7%)
Elemental Analysis: C, 83.20; H, 7.56; O, 9.24

The compound was purified by flash column chromatography using 0-40% hexanes in dichloromethane to afford 15% yield as a viscous yellow oil. $R_f$ = 0.69 (10% hexanes in dichloromethane). IR (neat): 3083, 3060, 3025, 2970, 2927, 2859, 2833, 1738, 1625, 1516, 1458, 1228, 1180, 838, 744 $cm^{-1}$. $^1H$ NMR (400 MHz, $CDCl_3$): δ = 7.57 (d, *J* = 8.6Hz, 1H), 7.46 (d, *J* = 8.2Hz, 1H), 7.11-6.94 (m, 8H), 4.81-4.76 (m, 1H), 3.79 (s, 3H), 2.80 (unresolved overlapping d, 2H), 2.66-2.58 (m , 1H), 2.38 (ddd, *J* = 14.3, 10.2, 4.5Hz, 1H), 2.22-2.13 (m, 1H), 2.00-1.91 (m, 1H), 1.38 (s, 3H), 1.03 (s, 3H). $^{13}C$ NMR (100 MHz, $CDCl_3$): δ = 158.26 (q), 142.96 (q), 134.87 (q), 133.43 (q), 130.19 (t), 128.81 (t), 128.43 (t), 127.80 (q), 127.63 (q), 126.05 (t), 125.77 (t), 120.57 (t), 117.62 (t), 101.94 (t), 70.92 (t), 70.66 (q), 55.55 (p), 38.22 (s), 36.93 (s), 31.11 (p), 30.86 (s), 23.57 (p). HRMS (CI): *m/z* $[M+Na]^+$ calcd for $C_{24}H_{26}O_2Na$: 369.1825; found: 369.1829.

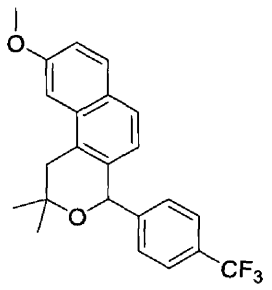
**9-methoxy-2,2-dimethyl-4-(4-nitrophenyl)-1,4-dihydro-2H-benzo-[f]isochromene (38a-2):**



Chemical Formula: $C_{22}H_{21}NO_4$
Exact Mass: 363.15
Molecular Weight: 363.41
m/z: 363.15 (100.0%), 364.15 (24.2%), 365.15 (3.6%)
Elemental Analysis: C, 72.71; H, 5.82; N, 3.85; O, 17.61

The compound was purified by flash column chromatography using 0-40% hexanes in dichloromethane to afford 22% yield as a viscous yellow oil. $R_f$ = 0.61 (pure dichloromethane). IR (neat): 3107, 3078, 3057, 2977, 2933, 2836, 1735, 1626, 1608, 1521, 1459, 1351, 1229, 1065, 837 $cm^{-1}$. $^1H$ NMR (400 MHz, $CDCl_3$): δ = 8.19 (d, *J* = 8.6Hz, 2H), 7.70 (d, *J* = 9.0Hz, 1H), 7.52 (d, *J* = 8.7Hz, 2H), 7.49 (d, *J* = 8.7Hz, 1H), 7.24 (d, *J* = 2.4Hz, 1H), 7.18 (dd, *J* = 8.8, 2.5Hz, 1H), 6.65 (d, *J* = 8.6Hz, 1H), 5.95 (s, 1H), 3.98 (s, 3H), 3.18 (d, *J* = 16.1Hz, 1H), 3.09 (d, *J* = 16.4Hz, 1H), 1.57 (s, 3H), 1.38 (s, 3H). $^{13}C$ NMR (100 MHz, $CDCl_3$): δ = 158.59 (q), 150.26 (q), 147.86 (q), 133.34 (q), 132.94 (q), 130.35 (t), 130.01 (t), 127.86 (q), 127.28 (q), 126.26 (t), 123.99 (t), 121.71 (t), 118.24 (t), 102.01 (t), 75.42 (t), 72.37 (q), 55.61 (p), 36.69 (s), 31.07 (p), 23.63 (p). HRMS (CI): *m/z* $[M+Na]^+$ calcd for $C_{22}H_{21}NO_4Na$: 386.1363; found: 386.1366.

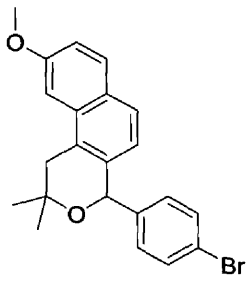
**9-methoxy-2,2-dimethyl-4-(4-(trifluoromethyl)phenyl)-1,4-dihydro-2H-benzo[f]isochromene (38a-3):**



Chemical Formula: $C_{23}H_{21}F_3O_2$
Exact Mass: 386.15
Molecular Weight: 386.41
m/z: 386.15 (100.0%), 387.15 (25.0%), 388.16 (3.0%)
Elemental Analysis: C, 71.49; H, 5.48; F, 14.75; O, 8.28

The compound was purified by flash column chromatography using 20-80% hexanes in dichloromethane to afford 25% yield as a yellow crystal. $R_f$ = 0.33 (40% hexanes in dichloromethane). IR (neat): 3058, 2999, 2980, 2932, 2906, 2836, 1925, 1627, 1516, 1332, 1230, 1168, 1068, 839 $cm^{-1}$. $^1H$ NMR (400 MHz, $CDCl_3$): δ = 7.70 (d, *J* = 8.9Hz, 1H), 7.58 (d, *J* = 8.2Hz, 2H), 7.49 (s, 1H), 7.46 (d, *J* = 8.6Hz, 2H), 7.24 (d, *J* = 2.3Hz, 1H), 7.17 (dd, *J* = 9.0, 2.4Hz, 1H), 6.68 (d, *J* = 8.6Hz, 1H), 5.90(s, 1H), 3.98 (s, 3H), 3.18 (d, *J* = 16.4Hz, 1H), 3.07 (d, *J* = 15.2Hz, 1H), 1.56 (s, 3H), 1.38 (s, 3H). $^{13}C$ NMR (100 MHz, $CDCl_3$): δ = 158.49 (q), 156.28 ($CF_3$, *J* = 210.6Hz), 146.98 (q), 133.63 (q), 133.30 (q), 130.54 (q), 130.33 (t), 129.54 (t), 127.82 (q), 127.26 (q), 126.08 (t), 125.72 (t), 122.06 (t), 118.06 (t), 102.01 (t), 75.76 (t), 72.18 (q), 55.59 (p), 36.75 (s), 31.14 (p), 23.63 (p).

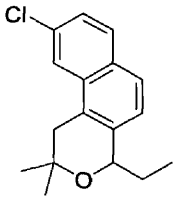
**4-(4-bromophenyl)-9-methoxy-2,2-dimethyl-1,4-dihydro-2H-benzo-[f]isochromene (38a-4):**




Chemical Formula: $C_{22}H_{21}BrO_2$
Exact Mass: 396.07
Molecular Weight: 397.31
m/z: 396.07 (100.0%), 398.07 (97.3%), 397.08 (24.1%), 399.07 (23.2%), 398.08 (3.2%), 400.08 (2.7%)
Elemental Analysis: C, 66.51; H, 5.33; Br, 20.11; O, 8.05

The compound was purified by flash column chromatography using 20-80% hexanes in dichloromethane to afford 29% yield as a viscous yellow oil. $R_f$ = 0.58 (40% hexanes in dichloromethane). IR (neat): 3054, 2974, 2931, 2836, 1905, 1700, 1626, 1515, 1228, 1071, 1011, 835, 738 $cm^{-1}$. $^1H$ NMR (400 MHz, $CDCl_3$): δ = 7.69 (d, *J* = 8.7Hz, 1H), 7.48 (s, 1H), 7.44 (dd, *J* = 10.7, 2.5Hz, 2H), 7.24-7.19 (m, 3H), 7.16 (dd, *J* = 8.8, 2.5Hz, 1H), 6.68 (d, *J* = 8.2Hz, 1H), 5.81 (s, 1H), 3.97 (s, 3H), 3.15 (d, *J* = 16.1Hz, 1H), 3.05 (d, *J* = 15.7Hz, 1H), 1.55 (s, 3H), 1.35 (s, 3H). $^{13}C$ NMR (100 MHz, $CDCl_3$): δ = 158.42 (q), 142.13 (q), 133.98 (q), 133.25 (q), 131.84 (t), 130.91 (t), 130.29 (t), 127.76 (q), 127.18 (q), 125.94 (t), 122.21 (t), 122.18 (q), 117.94 (t), 101.98 (t), 75.64 (t), 72.02 (q), 55.57 (p), 36.73 (s), 31.16 (p), 23.60 (p). HRMS (CI): *m/z* $[M+Na]^+$ calcd for $C_{22}H_{21}BrO_2Na$: 419.0617; found: 419.0618.

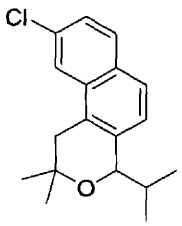
**9-chloro-4-ethyl-2,2-dimethyl-1,4-dihydro-2H-benzo[f]isochromene (38b-1):**




Chemical Formula: $C_{17}H_{19}ClO$
Exact Mass: 274.11
Molecular Weight: 274.79
m/z: 274.11 (100.0%), 276.11 (32.0%), 275.12 (18.6%), 277.11 (5.9%), 276.12 (1.8%)
Elemental Analysis: C, 74.31; H, 6.97; Cl, 12.90; O, 5.82

The compound was purified by flash column chromatography using 20-80% hexanes in dichloromethane to afford 39% yield as a viscous yellow oil. $R_f$ = 0.48 (40% hexanes in dichloromethane). IR (neat): 3052, 2972, 2932, 2874, 2831, 1903, 1724, 1623, 1597, 1505, 1367, 1202, 1096, 843 $cm^{-1}$. $^1H$ NMR (400 MHz, $CDCl_3$): δ = 7.88 (d, *J* = 2.0Hz, 1H), 7.72 (d, *J* = 8.6Hz, 1H), 7.63 (d, *J* = 8.6Hz, 1H), 7.38 (d, *J* = 8.6Hz, 1H), 7.21 (d, *J* = 8.6Hz, 1H), 4.91-4.88 (m, 1H), 2.92 (unresolved overlapping d, 2H), 2.09-1.99 (m, 1H), 1.90-1.80 (m, 1H), 1.47 (s, 3H), 1.15 (s, 3H), 0.80 (t, *J* = 7.5Hz, 3H). $^{13}C$ NMR (100 MHz, $CDCl_3$): δ = 135.55 (q), 133.11 (q), 132.31 (q), 130.53 (q), 130.17 (t), 128.60 (q), 126.21 (t), 126.03 (t), 123.32 (t), 122.27 (t), 72.32 (t), 70.51 (q), 36.63 (s), 30.97 (p), 29.08 (s), 23.46 (p), 8.74 (p).

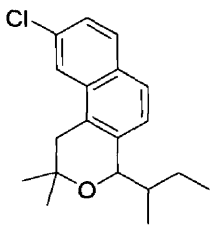
**9-chloro-4-isopropyl-2,2-dimethyl-1,4-dihydro-2H-benzo[f]isochromene (38b-2):**




Chemical Formula: $C_{18}H_{21}ClO$
Exact Mass: 288.13
Molecular Weight: 288.82
m/z: 288.13 (100.0%), 290.13 (34.0%), 289.13 (19.7%), 291.13 (6.3%)
Elemental Analysis: C, 74.86; H, 7.33; Cl, 12.27; O, 5.54

The compound was purified by flash column chromatography using 20-80% hexanes in dichloromethane to afford 27% yield as a viscous yellow oil. $R_f$ = 0.34 (80% hexanes in dichloromethane). IR (neat): 3053, 2973, 2930, 2871, 2827, 1623, 1595, 1504, 1366, 1197, 1048, 841, 630 $cm^{-1}$. $^1H$ NMR (400 MHz, $CDCl_3$): δ = 7.88 (d, *J* = 2.0Hz, 1H), 7.72 (d, *J* = 8.7Hz, 1H), 7.62 (d, *J* = 8.6Hz, 1H), 7.38 (dd, *J* = 8.8, 2.1Hz, 1H), 7.22 (d, *J* = 8.2Hz, 1H), 4.74 (d, *J* = 1.6Hz, 1H), 2.93 (dd, *J* = 16.0, 0.8Hz, 1H), 2.83 (d, *J* = 16.1Hz, 1H), 2.27 (sept. of d, *J* = 6.8, 2.4Hz, 1H), 1.44 (s, 3H), 1.13 (d, *J* = 7.0Hz, 3H), 1.09 (s, 3H), 0.57 (d, *J* = 6.7Hz, 3H). $^{13}C$ NMR (100 MHz, $CDCl_3$): δ = 135.88 (q), 133.06 (q), 132.22 (q), 130.48 (q), 130.14 (t), 128.90 (q), 126.11 (t), 125.92 (t), 123.34 (t), 122.29 (t), 75.86 (t), 70.13 (q), 36.59 (s), 33.97 (t), 30.92 (p), 23.37 (p), 20.13 (p), 15.00 (p).

**4-(sec-butyl)-9-chloro-2,2-dimethyl-1,4-dihydro-2H-benzo[f]isochromene (38b-3):**




Chemical Formula: $C_{19}H_{23}ClO$
Exact Mass: 302.14
Molecular Weight: 302.84
m/z: 302.14 (100.0%), 304.14 (32.0%), 303.15 (20.9%), 305.14 (6.6%), 304.15 (2.3%)
Elemental Analysis: C, 75.36; H, 7.66; Cl, 11.71; O, 5.28

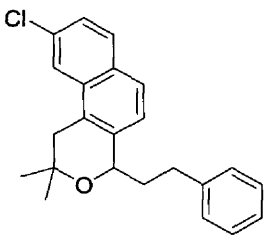
The compound was purified by flash column chromatography using 20-80% *n*-hexane in dichloromethane. A pair of diastereomers was obtained in 2:1 ratio with 36% total yield as viscous yellow oil. $R_f$ = 0.51 and 0.59 (70% *n*-hexane in dichloromethane). IR (neat): 3051, 2971, 2934, 2896, 2873, 2833, 2345, 1622, 1596, 1504, 1459, 1369, 1196, 840, 662 $cm^{-1}$.

Diastereomer A. ($R_f$ = 0.51). $^1H$ NMR (400 MHz, $CDCl_3$): δ = 7.90 (s, 1H), 7.75 (d, *J* = 8.6Hz, 1H), 7.65 (d, *J* = 8.6Hz, 1H), 7.40 (dd, *J* = 8.6, 2.0Hz, 1H), 7.24 (d, *J* = 8.6Hz, 1H), 4.88 (s, 1H), 2.95 (d, *J* = 16.0Hz, 1H), 2.86 (d, *J* = 16.0Hz, 1H), 2.02-1.95 (m, 1H), 1.72-1.60 (m, 1H), 1.51-1.47 (m, 1H), 1.45 (s, 3H), 1.12 (s, 3H), 1.02 (t, *J* = 7.4Hz, 3H), 0.56 (d, *J* = 7.0Hz, 3H). $^{13}C$ NMR (100 MHz, $CDCl_3$): δ = 136.02 (q), 133.07 (q), 132.20 (q), 130.41 (q), 130.14 (t), 128.96 (q), 126.06 (t), 125.92 (t), 123.34 (t), 122.25 (t), 73.73 (t), 70.02 (q), 40.76 (t), 36.52 (s), 30.93 (p), 27.00 (s), 23.31 (p), 12.86 (p), 12.62 (p).

Diastereomer B. ($R_f$ = 0.59). $^1H$ NMR (400 MHz, $CDCl_3$): δ = 7.90 (s, 1H), 7.75 (d, *J* = 8.6Hz, 1H), 7.65 (d, *J* = 8.2Hz, 1H), 7.40 (dd, *J* = 8.8, 1.7Hz, 1H), 7.24 (dd, *J* = 8.6, 3.1Hz, 1H), 4.81 (s, 1H), 2.95 (d, *J* = 15.6Hz, 1H), 2.86

(d, $J$ = 16.0Hz, 1H), 2.04-1.95 (m, 1H), 1.45 (broad s, 5H), 1.13 (s, 3H), 1.11 (s, 3H), 0.72 (t, $J$ = 7.4Hz, 3H). $^{13}$C NMR (100 MHz, $CDCl_3$): δ = 136.02 (q), 133.07 (q), 132.20 (q), 130.41 (q), 130.14 (t), 128.96 (q), 126.11 (t), 125.89 (t), 123.25 (t), 122.27 (t), 76.47 (t), 70.17 (q), 40.94 (t), 36.63 (s), 23.31 (p), 22.51 (s), 16.71 (p), 12.86 (p), 12.62 (p).

**9-chloro-2,2-dimethyl-4-phenethyl-1,4-dihydro-2H-benzo[f]isochromene (38b-4):**

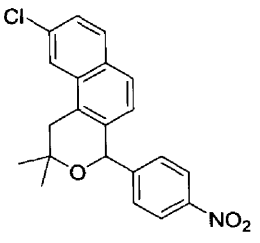



Chemical Formula: $C_{23}H_{23}ClO$
Exact Mass: 350.14
Molecular Weight: 350.89
m/z: 350.14 (100.0%), 352.14 (32.0%), 351.15 (25.2%), 353.14 (8.0%), 352.15 (3.2%), 354.15 (1.0%)
Elemental Analysis: C, 78.73; H, 6.61; Cl, 10.10; O, 4.56

The compound was purified by flash column chromatography using 20-80% hexanes in dichloromethane to afford 38% yield as a viscous yellow oil. $R_f$ = 0.54 (40% hexanes in dichloromethane). IR (neat): 3426, 3063, 3030, 2977, 2930, 2865, 2837, 1944, 1735, 1622, 1595, 1497, 1455, 1094, 838, 741 cm$^{-1}$. $^1$H NMR (400 MHz, $CDCl_3$): δ = 7.75 (d, $J$ = 1.5Hz, 1H), 7.59 (d, $J$ = 8.7Hz, 1H), 7.49 (d, $J$ = 8.7Hz, 1H), 7.25 (dd, $J$ = 9.0, 2.0Hz, 1H), 7.13-6.98 (m, 6H), 4.79-4.74 (m, 1H), 2.81 (s, 2H), 2.66-2.58 (m, 1H), 2.39 (ddd, $J$ =14.2, 10.0, 4.2Hz, 1H), 2.22-2.13 (m, 1H), 1.99-1.90 (m, 1H), 1.36 (s, 3H), 1.02 (s, 3H). $^{13}$C NMR (100 MHz, $CDCl_3$): δ = 142.75(q), 135.56 (q), 133.15 (q), 132.39 (q), 130.58 (q), 130.19 (t), 128.79 (t), 128.47 (q), 128.45 (t), 126.29 (t), 126.12 (t), 125.83

(t), 123.14 (t), 122.29 (t), 70.75 (t), 70.66 (q), 38.10 (s), 36.65 (s), 31.00 (p), 30.88 (s), 23.47 (p).

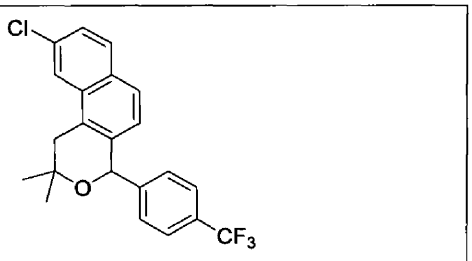
**9-chloro-2,2-dimethyl-4-(4-nitrophenyl)-1,4-dihydro-2H-benzo[f]isochromene (38b-5):**




Chemical Formula: $C_{21}H_{18}ClNO_3$
Exact Mass: 367.10
Molecular Weight: 367.83
m/z: 367.10 (100.0%), 369.09 (32.0%), 368.10 (23.0%), 370.10 (7.4%), 369.10 (3.2%), 371.10 (1.0%)
Elemental Analysis: C, 68.57; H, 4.93; Cl, 9.64; N, 3.81; O, 13.05

The compound was purified by flash column chromatography using 20-80% hexanes in dichloromethane to afford 45% yield as a viscous yellow oil. $R_f$ = 0.55 (40% hexanes in dichloromethane). IR (neat): 3110, 3079, 3056, 2975, 2931, 2870, 2455, 1927, 1798, 1725, 1609, 1526, 1352, 1270, 1187, 1075, 857, 742 $cm^{-1}$. $^1H$ NMR (400 MHz, $CDCl_3$): δ = 8.20 (dt, *J* = 8.6, 2.1Hz, 2H), 7.98 (d, *J* = 2.0Hz, 1H), 7.73 (d, *J* = 8.6Hz, 1H), 7.54-7.50 (m, 3H), 7.45 (dd, *J* = 8.8, 2.2Hz, 1H), 6.79 (d, *J* = 8.6Hz, 1H), 5.94 (s, 1H), 3.20 (d, *J* = 16.8Hz, 1H), 3.12 (dd, *J* = 16.4, 1.2Hz, 1H), 1.57 (s, 3H), 1.37 (s, 3H). $^{13}C$ NMR (100 MHz, $CDCl_3$): δ = 149.80 (q), 147.94 (q), 133.58 (q), 133.00 (q), 132.89 (q), 130.83 (q), 130.33 (t), 129.99 (t), 128.00 (q), 126.96 (t), 126.35 (t), 124.23 (t), 124.04 (t), 122.36 (t), 75.25 (t), 72.37 (q), 36.41 (s), 30.95 (p), 23.53 (p).

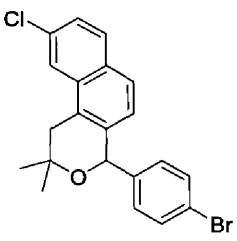
**9-chloro-2,2-dimethyl-4-(4-(trifluoromethyl)phenyl)-1,4-dihydro-2H-benzo[f]isochromene (38b-6):**




Chemical Formula: $C_{22}H_{18}ClF_3O$
Exact Mass: 390.10
Molecular Weight: 390.83
m/z: 390.10 (100.0%), 392.10 (32.2%), 391.10 (23.8%), 393.10 (7.7%), 392.11 (2.8%)
Elemental Analysis: C, 67.61; H, 4.64; Cl, 9.07; F, 14.58; O, 4.09

The compound was purified by flash column chromatography using 20-80% hexanes in dichloromethane to afford 48% yield as a viscous yellow oil. $R_f$ = 0.70 (40% hexanes in dichloromethane). IR (neat): 3054, 2976, 2930, 2871, 2853, 1922, 1737, 1619, 1594, 1502, 1416, 1323, 1164, 1128, 1068, 1019, 989, 838 $cm^{-1}$. $^1H$ NMR (400 MHz, $CDCl_3$): δ = 7.94 (d, *J* = 2.0Hz, 1H), 7.68 (d, *J* = 9.0Hz, 1H), 7.56 (d, *J* = 7.8Hz, 2H), 7.49 (d, *J* = 8.6Hz, 1H), 7.42 (d, *J* = 7.0Hz, 2H), 7.40 (dd, *J* = 8.6, 2.0Hz, 1H), 6.79 (d, *J* = 8.6Hz, 1H), 5.87 (s, 1H), 3.16 (d, *J* = 16.4Hz, 1H), 3.07 (dd, *J* = 16.5, 1.2Hz, 1H), 1.55 (s, 3H), 1.36 (s, 3H). $^{13}C$ NMR (100 MHz, $CDCl_3$): δ = 146.59 (q), 134.26 (q), 133.00 (q), 132.72 (q), 130.79 (q), 130.35 (q), 130.30 (t), 129.52 (t), 127.95 (q), 126.77 (t), 126.16 (t), 125.78 (t), 124.30 ($CF_3$, *J* = 272.1Hz), 124.59 (t), 122.35 (t), 75.59 (t), 72.15 (q), 36.44 (s), 31.00 (p), 23.50 (p).

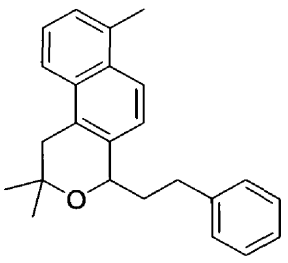
**4-(4-bromophenyl)-9-chloro-2,2-dimethyl-1,4-dihydro-2H-benzo[f]isochromene (38b-7):**




Chemical Formula: $C_{21}H_{18}BrClO$
Exact Mass: 400.02
Molecular Weight: 401.73
m/z: 402.02 (100.0%), 400.02 (77.4%), 404.02 (24.1%), 403.02 (22.7%), 401.03 (17.8%), 405.02 (5.5%), 404.03 (2.7%), 402.03 (2.1%)
Elemental Analysis: C, 62.79; H, 4.52; Br, 19.89; Cl, 8.82; O, 3.98

The compound was purified by flash column chromatography using 20-80% hexanes in dichloromethane to afford 61% yield as a viscous yellow oil. $R_f$ = 0.61 (40% hexanes in dichloromethane). IR (neat): 3050, 2972, 2931, 2897, 2840, 1903, 1732, 1619, 1592, 1501, 1485, 1366, 1264, 1184, 1094, 1069, 1009, 829, 736 $cm^{-1}$. $^1H$ NMR (400 MHz, $CDCl_3$): δ = 7.96 (s, 1H), 7.71 (d, *J* = 8.6Hz, 1H), 7.52-7.41 (m, 4H), 7.20 (d, *J* = 8.2Hz, 2H), 6.82 (d, *J* = 8.6Hz, 1H), 5.80 (s, 1H), 3.15 (d, *J* = 16.0Hz, 1H), 3.07 (d, *J* = 16.4Hz, 1H), 1.54 (s, 3H), 1.34 (s, 3H); $^{13}C$ NMR (100 MHz, $CDCl_3$): δ = 141.71 (q), 134.61 (q), 132.95 (q), 132.62 (q), 131.92 (t), 130.88 (t), 130.73 (q), 130.27 (t), 127.86 (q), 126.67 (t), 126.03 (t), 124.74 (t), 122.34 (q), 122.33 (t), 75.49 (t), 72.04 (q), 36.44 (s), 31.05 (p), 23.50 (p ). HRMS (CI): *m/z* $[M+Na]^+$ calcd for $C_{21}H_{18}BrClONa$: 423.0122; found: 423.0124.

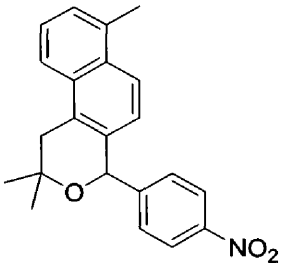
**2,2,7-trimethyl-4-phenethyl-1,4-dihydro-2H-benzo[f]isochromene (38c-1):**



Chemical Formula: $C_{24}H_{26}O$
Exact Mass: 330.20
Molecular Weight: 330.47
m/z: 330.20 (100.0%), 331.20 (26.3%), 332.21 (3.3%)
Elemental Analysis: C, 87.23; H, 7.93; O, 4.84

The compound was purified by flash column chromatography using 20-80% hexanes in dichloromethane to afford 57% yield as a viscous yellow oil. $R_f$ = 0.61 (40% hexanes in dichloromethane), $R_f$ = 0.45 (50% hexanes in dichloromethane). IR (neat): 3082, 3065, 3025, 296f8, 2922, 2861, 1960, 1740, 1694, 1602, 1454, 1379, 1097, 749, 701 $cm^{-1}$. $^1H$ NMR (400 MHz, $CDCl_3$): δ = 7.86 (d, *J* = 8.8Hz, 1H), 7.83 (d, *J* = 8.5Hz, 1H), 7.42 (dd, *J* = 8.4, 6.9Hz, 1H), 7.33-7.13 (m, 7H), 4.99-4.95 (m, 1H), 3.07 (d, *J* = 16.0Hz, 1H), 3.02 (d, *J* = 16.0Hz, 1H), 2.82-2.75 (m, 1H), 2.70 (s, 3H), 2.54 (ddd, *J* = 14.0, 10.1, 4.4Hz, 1H), 2.39-2.31 (m, 1H), 2.18-2.09 (m, 1H), 1.52 (s, 3H), 1.18 (s, 3H). $^{13}C$ NMR (100 MHz, $CDCl_3$): δ=142.95 (q), 135.05 (q), 133.95 (q), 132.37 (q), 131.43 (q), 129.57 (q), 128.81 (t), 128.43 (t), 126.39 (t), 126.02 (t), 125.77 (t), 122.62 (t), 122.43 (t), 121.24 (t), 70.84 (t), 70.75 (q), 38.22 (s), 37.00 (s), 31.09 (p), 30.84 (s), 23.51 (p), 19.86 (p). HRMS (CI): *m/z* $[M+Na]^+$ calcd for $C_{24}H_{26}ONa$: 353.1876; found: 353.1878.

**2,2,7-trimethyl-4-(4-nitrophenyl)-1,4-dihydro-2H-benzo[f]isochromene (38c-2):**

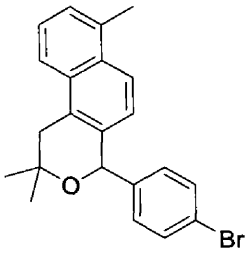



Chemical Formula: $C_{22}H_{21}NO_3$
Exact Mass: 347.15
Molecular Weight: 347.41
m/z: 347.15 (100.0%), 348.16 (24.2%), 349.16 (3.4%)
Elemental Analysis: C, 76.06; H, 6.09; N, 4.03; O, 13.82

The compound was purified by flash column chromatography using 20-80% hexanes in dichloromethane and then 70% hexanes in ethyl acetate to afford 46% yield as a viscous yellow oil.

$R_f$ = 0.34 (40% hexanes in dichloromethane), $R_f$ = 0.69 (70% hexanes in ethyl acetate). IR (neat): 3071, 2973, 2931, 2893, 2860, 1601, 1520, 1346, 1182, 1072, 846, 798 $cm^{-1}$. $^1H$ NMR (400 MHz, $CDCl_3$): δ = 8.18 (d, *J* = 9.0Hz, 2H), 7.87 (d, *J* = 8.2Hz, 1H), 7.73 (d, *J* = 8.6Hz, 1H), 7.52 (d, *J* = 9.0Hz, 2H), 7.47 (t, *J* = 7.8Hz, 1H), 7.34 (d, *J* = 7.0Hz, 1H), 6.82 (d, *J* = 9.0Hz, 1H), 5.96(s, 1H), 3.22 (overlapping d, *J* = 17.6Hz, 2H), 2.64 (s, 3H), 1.56 (s, 3H), 1.37 (s, 3H). $^{13}C$ NMR (100 MHz, $CDCl_3$): δ = 150.25 (q), 147.86 (q), 135.27 (q), 132.22 (q), 132.06 (q), 131.68 (q), 130.00 (t), 129.04 (q), 127.02 (t), 126.49 (t), 124.00 (t), 123.72 (t), 122.67 (t), 121.25 (t), 75.32 (t), 72.44 (q), 36.76 (s), 31.04 (p), 23.56 (p), 19.80 (p).

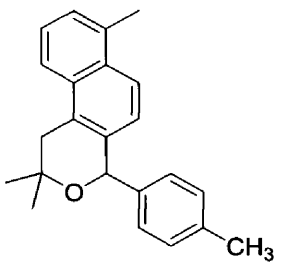
**4-(4-bromophenyl)-2,2,7-trimethyl-1,4-dihydro-2H-benzo[f]isochromene (38c-3):**




Chemical Formula: $C_{22}H_{21}BrO$
Exact Mass: 380.08
Molecular Weight: 381.31
m/z: 382.08 (100.0%), 380.08 (99.8%), 381.08 (24.0%), 383.08 (23.4%), 384.08 (2.8%)
Elemental Analysis: C, 69.30; H, 5.55; Br, 20.95; O, 4.20

The compound was purified by flash column chromatography using 20-80% hexanes in dichloromethane to afford 62% yield as a viscous yellow oil. $R_f$ = 0.60 (40% hexanes in dichloromethane). IR (neat): 3073, 3046, 2991, 2937, 2899, 2871, 2843, 2340, 1906, 1737, 1602, 1488, 1382, 1272, 1187, 1080, 817, 774 $cm^{-1}$. $^1H$ NMR (400 MHz, $CDCl_3$): δ = 7.87 (d, *J* = 8.6Hz, 1H), 7.72 (d, *J* = 9.0Hz, 1H), 7.47-7.43 (m, 3H), 7.33 (d, *J* = 6.6Hz, 1H), 7.20 (d, *J* = 8.2Hz, 2H), 6.86 (d, *J* = 8.6Hz, 1H), 5.82 (s, 1H), 3.18 (unresolved overlapping d, 2H), 2.64 (s, 3H), 1.54 (s, 3H), 1.34 (s, 3H). $^{13}C$ NMR (100 MHz, $CDCl_3$): δ = 142.11 (q), 135.17 (q), 133.10 (q), 132.16 (q), 131.86 (t), 131.56 (q), 130.90 (t), 128.90 (q), 126.76 (t), 126.27 (t), 124.22 (t), 122.34 (t), 122.20 (q), 121.24 (t), 75.54 (t), 72.09 (q), 36.79 (s), 31.14 (p), 23.53 (p), 19.83 (p).

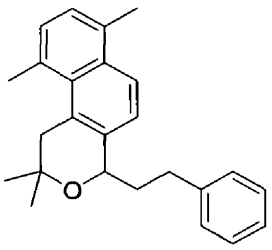
**2,2,7-trimethyl-4-(p-tolyl)-1,4-dihydro-2H-benzo[f]isochromene (38c-4):**



Chemical Formula: $C_{23}H_{24}O$
Exact Mass: 316.18
Molecular Weight: 316.44
m/z: 316.18 (100.0%), 317.19 (25.2%), 318.19 (3.2%)
Elemental Analysis: C, 87.30; H, 7.64; O, 5.06

The compound was purified by flash column chromatography using 20-80% hexanes in dichloromethane to afford 74% yield as a viscous yellow oil. $R_f$ = 0.61 (40% hexanes in dichloromethane). IR (neat): 3068, 3024, 2987, 2937, 2893, 2864, 2833, 1601, 1509, 1439, 1379, 1301, 1265, 1177, 1068, 1020 $cm^{-1}$. $^1H$ NMR (400 MHz, $CDCl_3$): δ = 7.87 (d, *J* = 8.6Hz, 1H), 7.70 (d, *J* = 9.0Hz, 1H), 7.43 (dd, *J* = 8.6, 7.1Hz, 1H), 7.31 (d, *J* = 7.1Hz, 1H), 7.21 (d, *J* = 7.9Hz, 2H), 7.12 (d, *J* = 7.9Hz, 2H), 6.91 (d, *J* = 9.0Hz, 1H), 5.83 (s, 1H), 3.20 (d, *J* = 16.5Hz, 1H), 3.15 (d, *J* = 16.1Hz, 1H), 2.63 (s, 3H), 2.31 (s, 3H), 1.53 (s, 3H), 1.34 (s, 3H); $^{13}C$ NMR (100 MHz, $CDCl_3$): δ = 140.15 (q), 137.84 (q), 135.09 (q), 134.02 (q), 132.19 (q), 131.50 (q), 129.40 (t), 129.11 (t), 128.83 (q), 126.54 (t), 126.08 (t), 124.56 (t), 122.12 (t), 121.26 (t), 75.93 (t), 71.84 (q), 36.89 (s), 31.24 (p), 23.56 (p), 21.41 (p), 19.81 (p). HRMS (CI): *m/z* $[M+Na]^+$ calcd for $C_{23}H_{24}ONa$: 339.1719; found: 339.1722.

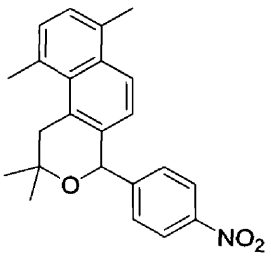
**2,2,7,10-tetramethyl-4-phenethyl-1,4-dihydro-*2H*-benzo[*f*]isochromene (38d-1):**



Chemical Formula: $C_{25}H_{28}O$
Exact Mass: 344.21
Molecular Weight: 344.50
m/z: 344.21 (100.0%), 345.22 (27.4%), 346.22 (3.8%)
Elemental Analysis: C, 87.16; H, 8.19; O, 4.64

The compound was purified by flash column chromatography using 20-80% hexanes in dichloromethane to afford 78% yield as a viscous yellow oil. $R_f$ = 0.58 (40% hexanes in dichloromethane). IR (neat): 3086, 3061, 3029, 2978, 2929, 2861, 1736, 1602, 1497, 1454, 1366, 1097, 823, 741 $cm^{-1}$. $^1H$ NMR (400 MHz, $CDCl_3$): δ = 7.83 (d, *J* = 9.0Hz, 1H), 7.26-7.12 (m, 8H), 4.98 (dd, *J* = 3.3, 1.8Hz, 1H), 3.40 (d, *J* = 16.0Hz, 1H), 3.19 (dd, *J* = 15.9Hz, 0.9Hz, 1H), 2.85 (s, 3H), 2.83-2.77 (m, 1H), 2.63 (s, 3H), 2.56 (ddd, *J* = 14.5, 10.6, 4.6Hz, 1H), 2.34-2.25 (m, 1H), 2.15-2.06 (m, 1H), 1.48 (s, 3H), 1.04 (s, 3H); $^{13}C$ NMR (100 MHz, $CDCl_3$): δ = 142.91 (q), 135.30 (q), 133.71 (q), 133.08 (q), 132.98 (q), 132.84 (q), 131.25 (q), 130.13 (t), 128.79 (t), 128.41 (t), 126.13 (t), 125.75 (t), 121.31 (t), 122.68 (t), 72.03 (t), 70.89 (q), 42.59 (s), 38.98(s), 31.23 (p), 30.80 (s), 26.45 (p), 22.83 (p), 20.28 (p). HRMS (CI): *m/z* $[M+Na]^+$ calcd for $C_{25}H_{28}ONa$: 367.2032; found: 367.2036.

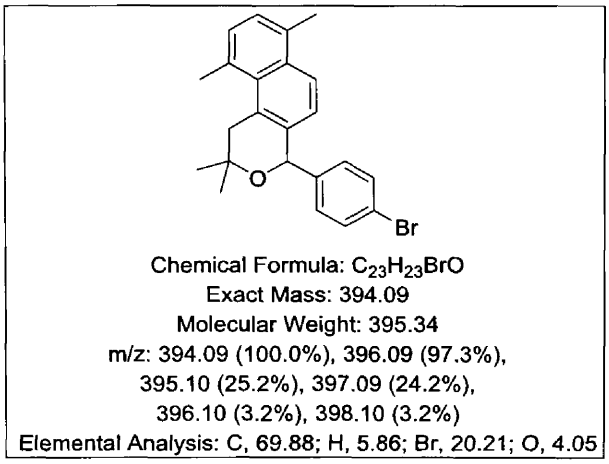
**2,2,7,10-tetramethyl-4-(4-nitrophenyl)-1,4-dihydro-*2H*-benzo[*f*]iso-chromene (38d-2):**



Chemical Formula: $C_{23}H_{23}NO_3$
Exact Mass: 361.17
Molecular Weight: 361.44
m/z: 361.17 (100.0%), 362.17 (25.3%), 363.17 (3.7%)
Elemental Analysis: C, 76.43; H, 6.41; N, 3.88; O, 13.28

The compound was prepared according to General Procedure B and purified by flash column chromatography using a mixture of 20-80% hexanes in dichloromethane and 80% hexanes in ethyl acetate to afford 53% yield as a viscous yellow oil. $R_f$ = 0.48 (a mixture of 80% hexanes in dichloromethane and 80% hexanes in ethyl acetate). IR (neat): 3107, 3078, 3036, 2978, 2935, 2860, 2367, 1738, 1607, 1559, 1526, 1457, 1340 $cm^{-1}$. $^1H$ NMR (400 MHz, $CDCl_3$): δ = 8.16 (d, *J* = 9.0Hz, 2H), 7.73 (d, *J* = 9.0Hz, 1H), 7.54 (d, *J* = 9.0Hz, 2H), 7.22 (d, *J* = 7.4Hz, 1H), 7.17 (d, *J* = 7.5Hz, 1H), 6.84 (d, *J* = 9.0Hz, 1H), 5.97 (s, 1H), 3.59 (d, *J* = 16.5Hz, 1H), 3.37 (d, *J* = 16.4Hz, 1H), 2.92 (s, 3H), 2.58 (s, 3H), 1.51 (s, 3H), 1.24 (s, 3H). $^{13}C$ NMR (100 MHz, $CDCl_3$): δ = 150.37 (q), 147.79 (q), 133.63 (q), 133.30 (q), 133.19 (q), 133.12 (q), 132.09 (q), 130.74 (q), 130.65 (t), 129.87 (t), 126.76 (t), 124.00 (t), 123.67 (t), 123.53 (t), 76.24 (t), 72.45 (q), 42.19 (s), 31.17 (p), 26.58 (p), 22.96 (p), 20.22 (p). HRMS (CI): *m/z* $[M+Na]^+$ calcd for $C_{23}H_{23}NO_3Na$: 384.1570; found: 384.1574.

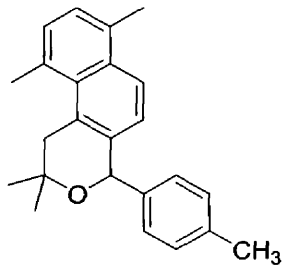
**4-(4-bromophenyl)-2,2,7,10-tetramethyl-1,4-dihydro-*2H*-benzo[*f*]iso-chromene (38d-3):**




Chemical Formula: $C_{23}H_{23}BrO$
Exact Mass: 394.09
Molecular Weight: 395.34
m/z: 394.09 (100.0%), 396.09 (97.3%), 395.10 (25.2%), 397.09 (24.2%), 396.10 (3.2%), 398.10 (3.2%)
Elemental Analysis: C, 69.88; H, 5.86; Br, 20.21; O, 4.05

The compound was prepared according to General Procedure B and purified by flash column chromatography using 20-80% hexanes in dichloromethane to afford 77% yield as light yellow crystals. $R_f$ = 0.60 (40% hexanes in dichloromethane). IR (neat): 3043, 2973, 2928, 2859, 2839, 1906, 1860, 1591, 1579, 1486, 1366, 1184, 1071, 1011, 824 $cm^{-1}$. $^1H$ NMR (400 MHz, $CDCl_3$): δ = 7.71 (d, *J* = 9.0Hz, 1H), 7.43 (d, *J* = 8.2Hz, 2H), 7.24-7.15 (m, 4H), 6.86 (d, *J* = 9.0Hz, 1H), 5.83 (s, 1H), 3.57 (d, *J* = 16.0Hz, 1H), 3.33 (d, *J* = 15.6Hz, 1H), 2.90 (s, 3H), 2.57 (s, 3H), 1.49 (s, 3H), 1.21 (s, 3H). $^{13}C$ NMR (100 MHz, $CDCl_3$): δ = 142.20 (q), 134.09 (q), 133.54 (q), 133.23 (q), 133.09 (q), 133.07 (q), 131.85 (t), 130.82 (t), 130.58 (q), 130.44 (t), 126.51 (t), 124.01 (t), 123.34 (t), 122.14 (q), 76.44 (t), 72.12 (q), 42.24 (s), 31.28 (p), 26.62 (p), 22.90 (p), 20.27 (p).

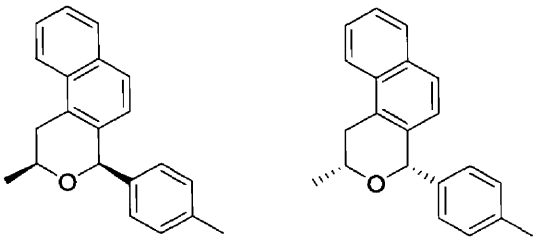
**2,2,7,10-tetramethyl-4-(p-tolyl)-1,4-dihydro-2*H*-benzo[*f*]isochromene (38d-4):**



Chemical Formula: $C_{24}H_{26}O$
Exact Mass: 330.20
Molecular Weight: 330.47
m/z: 330.20 (100.0%), 331.20 (26.3%), 332.21 (3.3%)
Elemental Analysis: C, 87.23; H, 7.93; O, 4.84

Prepared according to General Procedure B, this compound was purified by flash column chromatography using 20-80% hexanes in dichloromethane to afford 89% yield as light yellow solid. $R_f$ = 0.58 (40% hexanes in dichloromethane). IR (neat): 3024, 2968, 2924, 2860, 2833, 1514, 1452, 1379, 1366, 1300, 1179, 1082, 1058, 820 $cm^{-1}$. $^1H$ NMR (400 MHz, $CDCl_3$): δ = 7.69 (d, *J* = 8.8Hz, 1H), 7.24-7.10 (m, 6H), 6.91 (d, *J* = 8.5Hz, 1H), 5.84 (s, 1H), 3.58 (d, *J* = 16.2Hz, 1H), 3.32 (d, *J* = 16.2Hz, 1H), 2.90 (s, 3H), 2.56 (s, 3H), 2.30 (s, 3H), 1.48 (s, 3H), 1.21 (s, 3H). $^{13}C$ NMR (100 MHz, $CDCl_3$): δ = 140.21 (q), 137.78 (q), 135.00 (q), 133.55 (q), 133.16 (q), 133.09 (q), 132.98 (q), 130.50 (q), 130.25 (t), 129.40 (t), 129.01 (t), 126.29 (t), 124.35 (t), 123.12 (t), 76.83 (t), 71.89 (q), 42.36 (s), 31.37 (p), 26.61 (p), 22.91 (p), 21.39 (p), 20.25 (p). HRMS (CI): *m/z* $[M+Na]^+$ calcd for $C_{24}H_{26}ONa$: 353.1876; found: 353.1877.

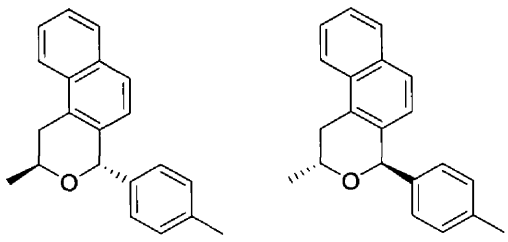
**(2*S*,4*R*)-2-methyl-4-(*p*-tolyl)-1,4-dihydro-2*H*-benzo[*f*]isochromene (42a) and (2*R*,4*S*)-2-methyl-4-(*p*-tolyl)-1,4-dihydro-2*H*-benzo[*f*]isochromene (42b):**



Chemical Formula: $C_{21}H_{20}O$
Exact Mass: 288.15
Molecular Weight: 288.39
m/z: 288.15 (100.0%), 289.15 (22.7%), 290.16 (2.7%)
Elemental Analysis: C, 87.46; H, 6.99; O, 5.55

The compound was purified by flash column chromatography using 20-80% *n*-hexane in dichloromethane to afford a pair of diastereomers in 81% combined yield, The *cis* diastereomer was obtained in 45% yield as light yellow crystal. $R_f$ = 0.43 (50% *n*-hexane in dichloromethane). IR (neat): 3421, 3301, 3052, 3023, 2971, 2926, 2892, 2365, 1916, 1713, 1511, 1456, 1386, 1257, 1118, 948 $cm^{-1}$. $^1H$ NMR (400 MHz, $CDCl_3$): δ = 7.96 (d, *J* = 8.2Hz, 1H), 7.75 (d, *J* = 8.6Hz, 1H), 7.55-7.43 (m, 3H), 7.20 (d, *J* = 8.2Hz, 2H), 7.13 (d, *J* = 8.2Hz, 2H), 6.82 (d, *J* = 8.6Hz, 1H), 5.83 (s, 1H), 4.13-4.05 (m, 1H), 3.21 (unresolved d of m, *J* = 16.1Hz, 1H), 3.05 (APP ddd, *J* = 16.1, 10.5, 2.0Hz, 1H), 2.32 (s, 3H), 1.50 (d, *J*= 6.2Hz, 3H). $^{13}C$ NMR (100 MHz, $CDCl_3$): δ = 139.65 (q), 138.04 (q), 135.27 (q), 132.32 (q), 131.80 (q), 129.51 (q), 129.43 (t), 129.12 (t), 128.63 (t), 126.43 (t), 126.13 (t), 125.67 (t), 124.90 (t), 123.06 (t), 81.30 (t), 71.14 (t), 33.38 (s), 22.35 (p), 21.42 (p). HRMS (CI): *m/z* $[M+Na]^+$ calcd for $C_{21}H_{20}ONa$: 311.1406; found: 311.1409.

**(*2S,4S*)-2-methyl-4-(p-tolyl)-1,4-dihydro-*2H*-benzo[*f*]isochromene (42c) and (*2R,4R*)-2-methyl-4-(*p*-tolyl)-1,4-dihydro-*2H*-benzo[*f*]isochromene (42d):**



Chemical Formula: $C_{21}H_{20}O$
Exact Mass: 288.15
Molecular Weight: 288.39
m/z: 288.15 (100.0%), 289.15 (22.7%), 290.16 (2.7%)
Elemental Analysis: C, 87.46; H, 6.99; O, 5.55

The *trans* diastereomer was isolated in 36% yield as a viscous yellow oil. $R_f$ = 0.29 (50% *n*-hexane in dichloromethane). IR (neat): 3052, 2972, 2923, 2892, 1917, 1511, 1446, 1387, 1119, 1062, 817, 769 $cm^{-1}$. $^1H$ NMR (400 MHz, $CDCl_3$): δ = 7.98 (d, *J*= 8.6Hz, 1H), 7.84 (dd, *J* = 7.8, 1.6Hz, 1H), 7.64 (d, *J* = 8.6Hz, 1H), 7.57-7.48 (m, 2H), 7.15 (d, *J* = 8.2Hz, 2H), 7.11 (d, *J* = 8.2Hz, 2H), 7.05 (d, *J* = 8.2Hz, 1H), 6.01 (s, 1H), 4.00 (dd of quartets, *J* = 10.2, 6.3, 3.6Hz, 1H), 3.21 (dd, *J* = 16.6, 3.7Hz, 1H), 2.92 (dd, *J* = 16.8, 10.2Hz, 1H), 2.33 (s, 3H), 1.34 (d, *J* = 6.3Hz, 3H). $^{13}C$ NMR (100 MHz, $CDCl_3$) (two aromatic quaternary carbons are overlapped): δ = 139.20 (q), 137.81 (q), 132.70 (q), 132.11 (q), 129.91 (q), 129.67 (t), 129.04 (t), 128.81 (t), 126.46 (t), 126.01 (t), 125.80 (t), 125.51 (t), 122.96 (t), 77.56 (t), 63.75 (t), 32.75 (s), 21.95 (p), 21.36 (p).

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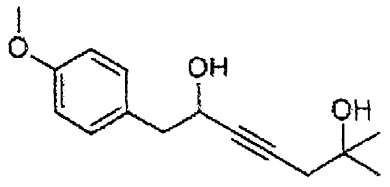
34. Result was from : Nofi, C. P.

*Supporting information for:*

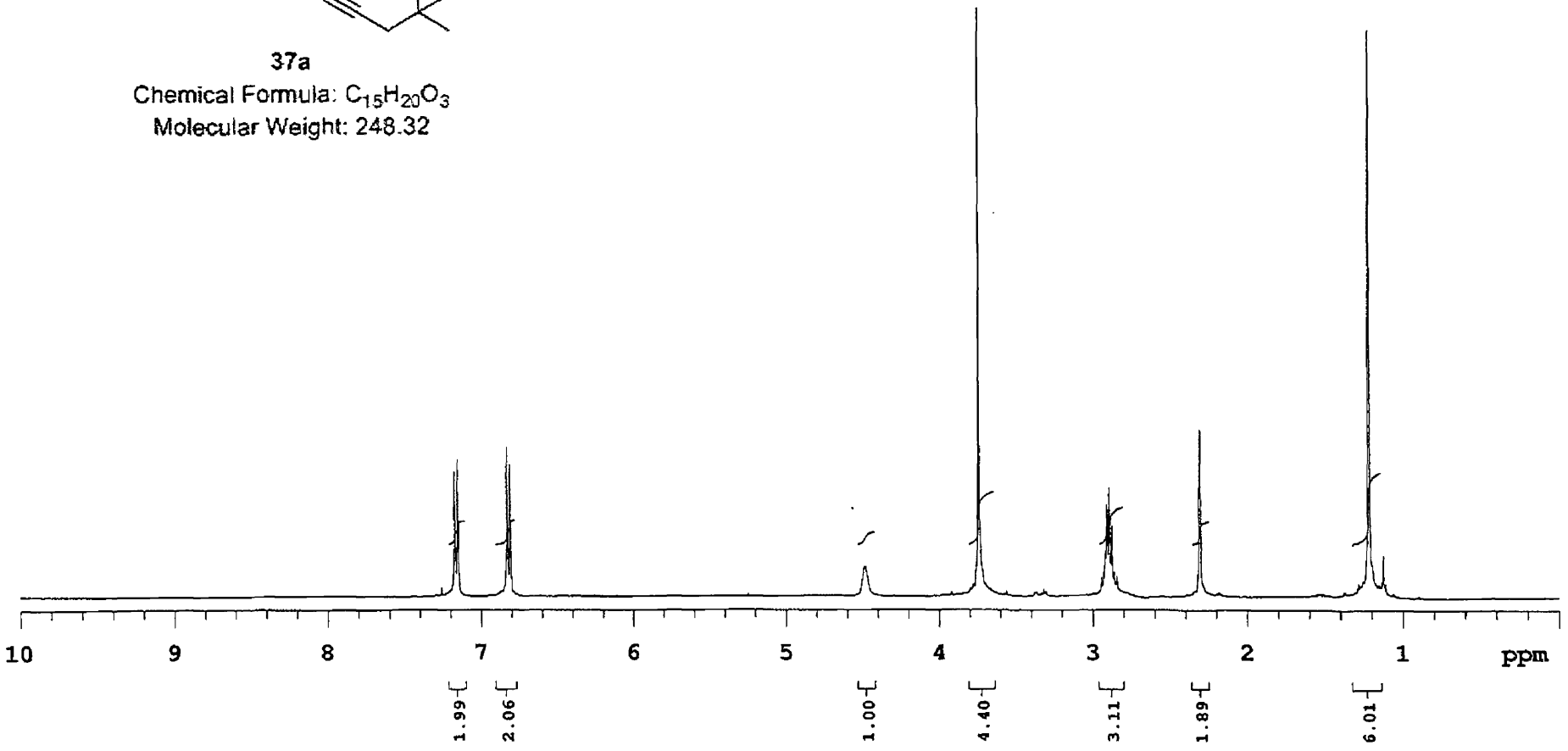
# Two-Component, Four Reaction Domino Sequence toward Novel Tricyclic 1,4-dihydro-*2H*-benzo[*f*]isochromenes.




**37a**

Chemical Formula: $C_{15}H_{20}O_3$

Molecular Weight: 248.32

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|---|---|---|---|---|
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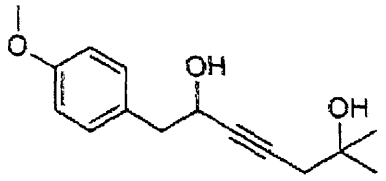
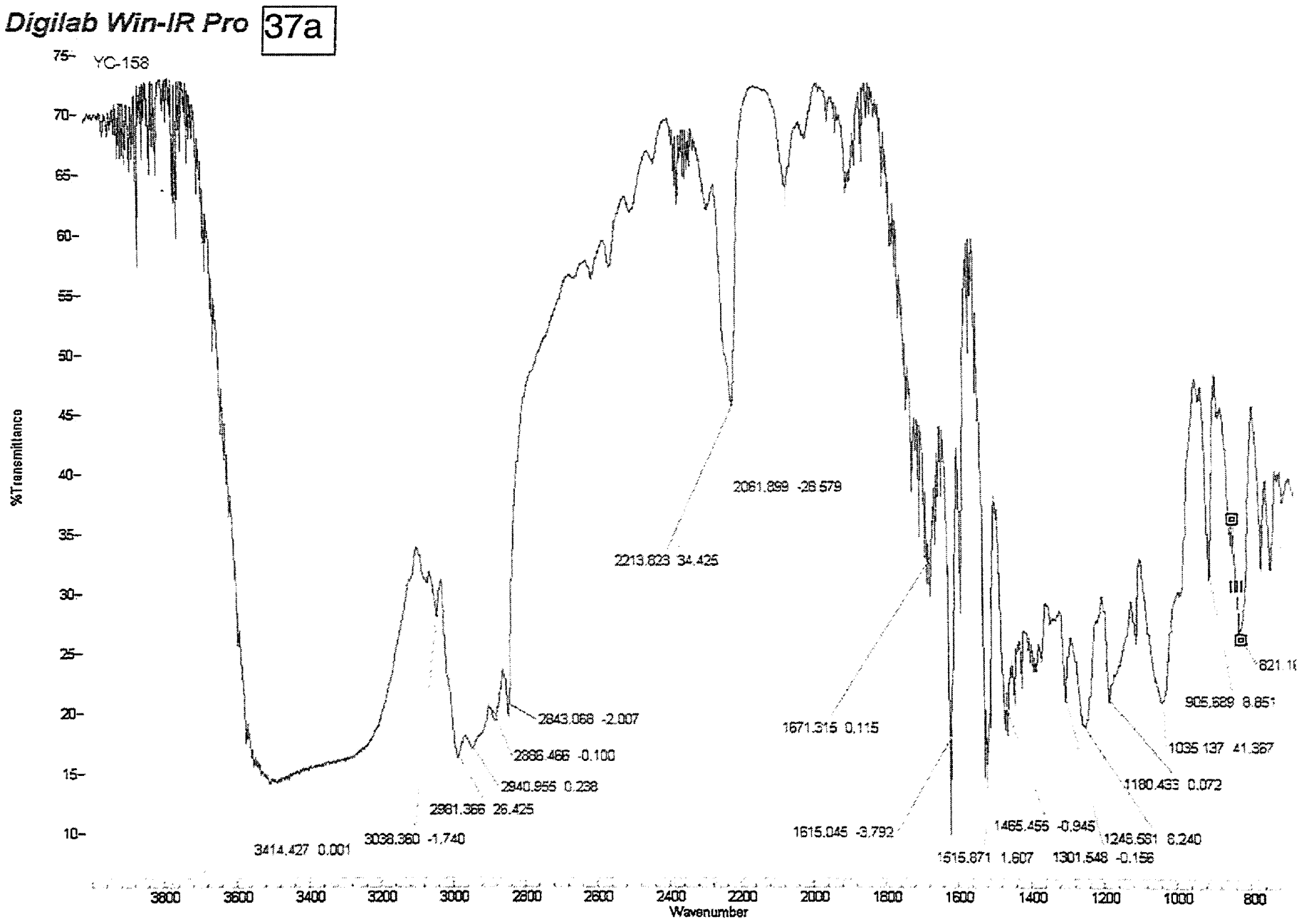
YC-90 pure 1-(4-methoxyphenyl)-6-methylhept-3-yne-2,6-diol; CDCl3; 8/28/2013

Sample Name:
yc-90




**37a**

Chemical Formula: $C_{15}H_{20}O_3$
Molecular Weight: 248.32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YC-158
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# Mass Spectrum List Report



**Analysis Info**

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| Method | XMASS_Method | Operator | FTMS_USER |
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| | YC-158_pos: in 1:1 THF:MeOH w/ NaCl.. | | |

**Acquisition Parameter**

**Sample: YC-158**
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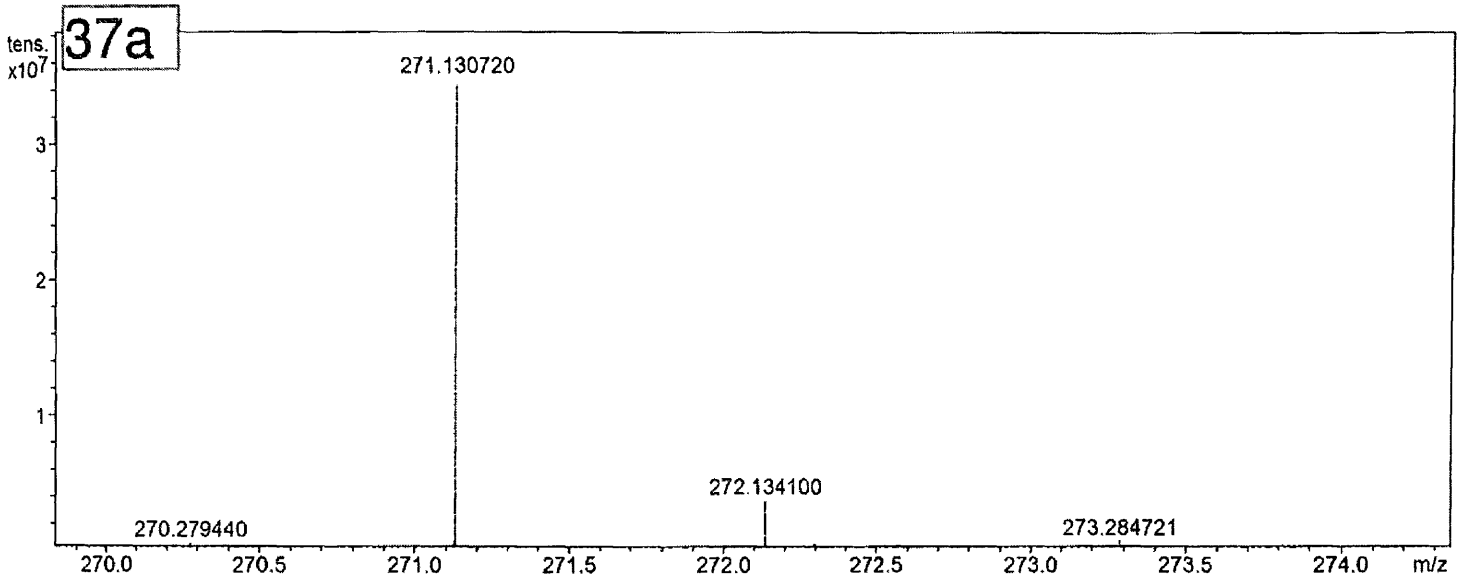
**Observed Mass = 271.130720u**
**Difference = 1.0 ppm**

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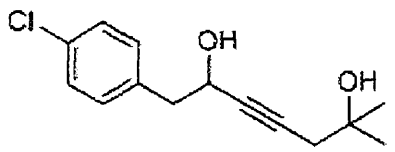
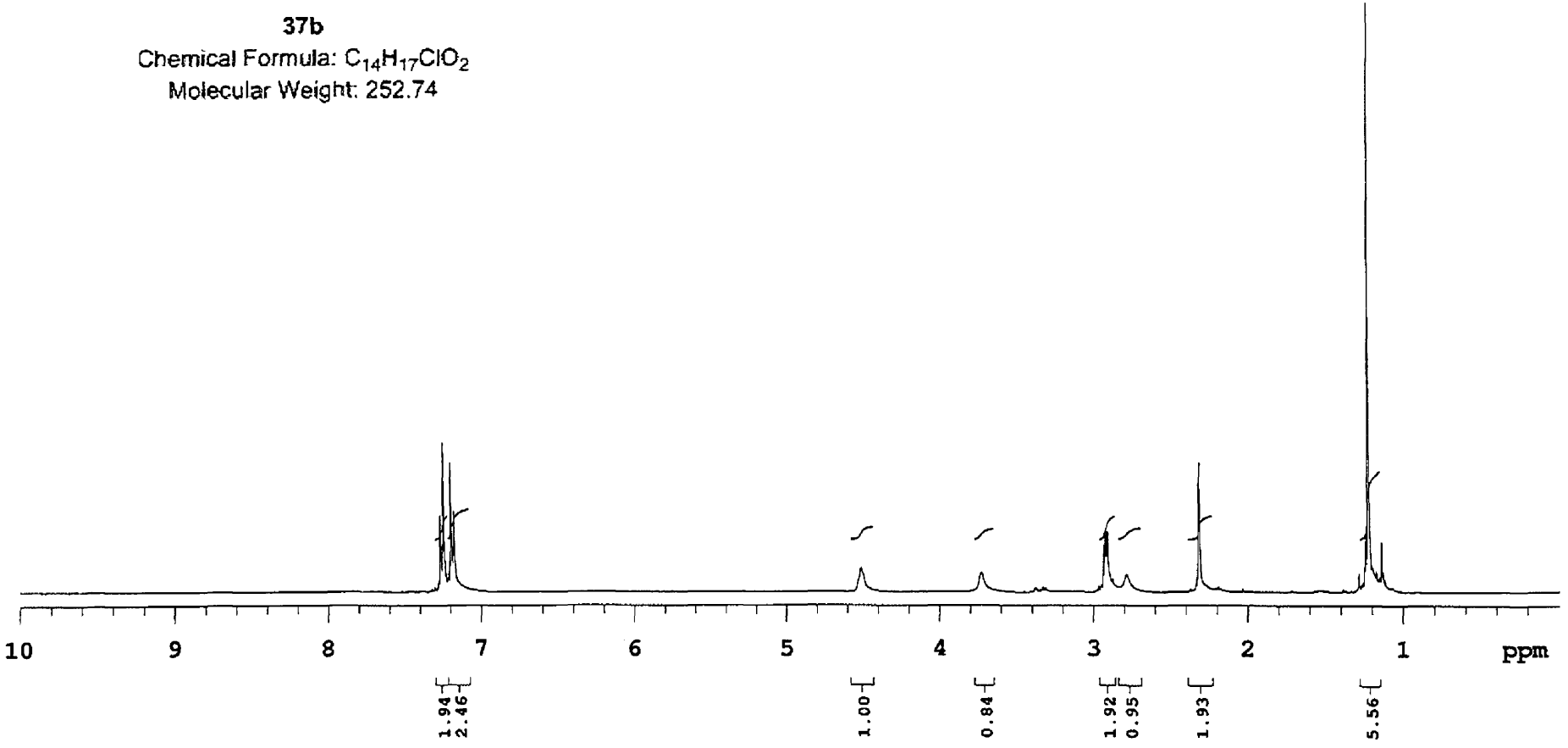
| 560.364724 | 19041199 |
| 567.281971 | 27675609 |
| 595.382447 | 26979480 |
| 596.385929 | 5858463 |
| 611.308216 | 10640660 |
| 631.419053 | 5836220 |
| 639.408903 | 12221951 |
| 655.334700 | 5252739 |
| 683.435132 | 4967254 |
| 685.434281 | 7335779 |
| 685.436441 | 50638691 |
| 686.439991 | 15142762 |




**37b**

Chemical Formula: $C_{14}H_{17}ClO_2$

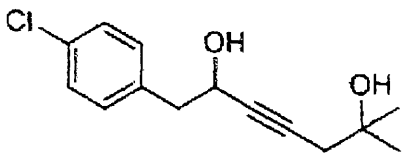
Molecular Weight: 252.74




| | | | | |
|---|---|---|---|---|
| PULSE SEQUENCE<br>Relax. delay 1.000 sec<br>Pulse 14.9 degrees<br>Acq. time 1.998 sec<br>Width 6402.0 Hz<br>8 repetitions | OBSERVE H1, 400.1766762 | DATA PROCESSING<br>FT size 32768<br>Total time 1 minute | | YC-88 pure; cl-sub. alkynediol; CDCl3; 8/31/2013<br>Solvent: cdcl3<br>Ambient temperature<br>Operator: rjhink<br>File: YC-88-h |

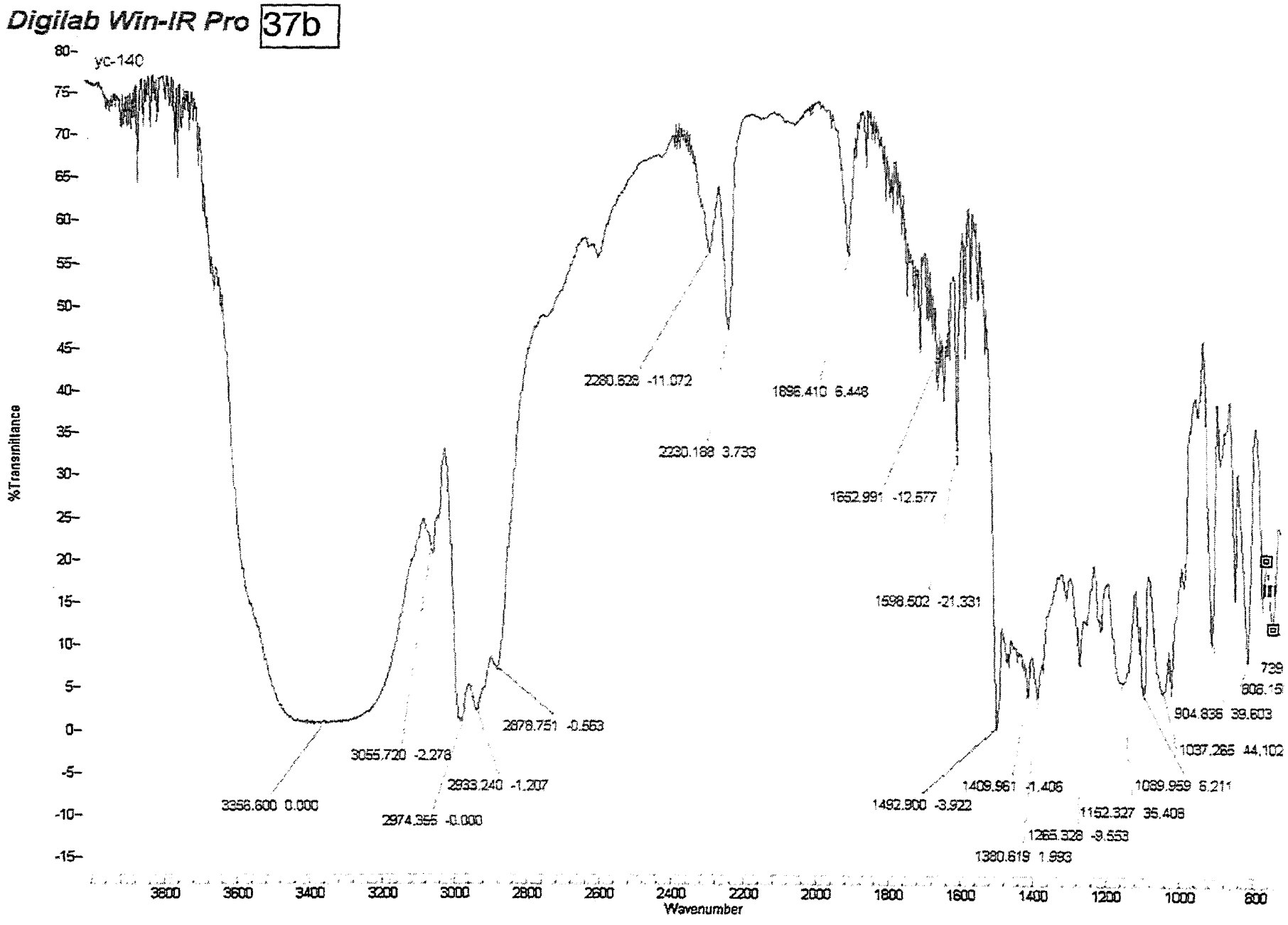
YC-88 cl-sub. alkynediol; CDCl3; 8/31/2013

Sample Name:
yc-88




**37b**

Chemical Formula: $C_{14}H_{17}ClO_2$
Molecular Weight: 252.74


Digilab Win-IR Pro 37b
yc-140
%Transmittance
Wavenumber
3356.600 0.000
3055.720 -2.278
2974.355 -0.000
2933.240 -1.207
2878.751 -0.563
2280.628 -11.072
2230.188 3.733
1696.410 6.448
1652.991 -12.577
1598.502 -21.331
1492.900 -3.922
1409.961 -1.406
1380.619 1.993
1265.328 -9.553
1152.327 35.406
1089.959 6.211
1037.265 44.102
904.836 39.603
739
806.15

# Mass Spectrum List Report

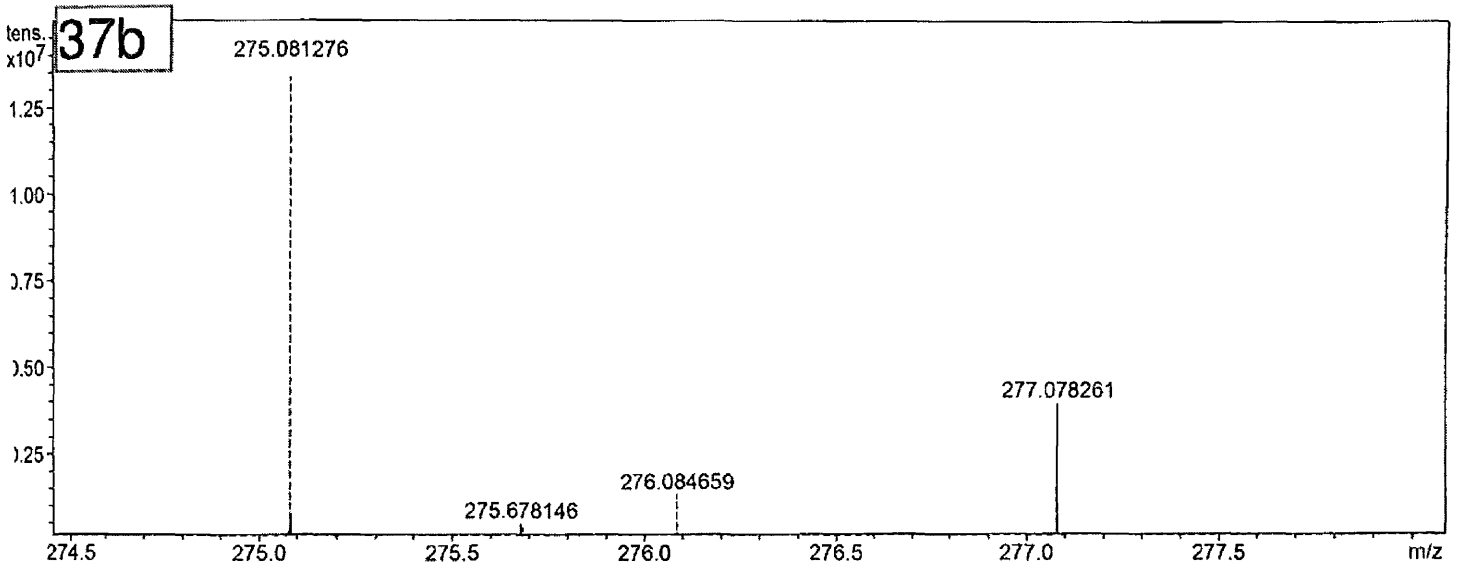


**Analysis Info**

| | | | |
|---|---|---|---|
| Analysis Name | YC-140_pos_000001.d | Acquisition Date | 7/22/2014 1:40:19 PM |
| Method | XMASS_Method | Operator | FTMS_USER |
| Sample Name: | YC-140_pos | Instrument | apex-Qe |
| | YC-140_pos: in 1:1 THF:MeOH w/ NaCl. (re-tune) | | |

**Acquisition Parameter**

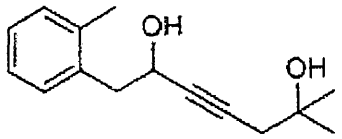
**Sample: YC-140**
**Exact Mass of = (C14H17ClO2)Na+ : 275.080929u**
**Observed Mass = 275.081276u**
**Difference = 1.3 ppm**




| m/z | I |
|---|---|
| 168.041034 | 11980777 |
| 204.031831 | 11470152 |
| 275.081276 | 13758114 |
| 288.289954 | 124871465 |
| 289.293381 | 16405300 |
| 292.768337 | 12054362 |
| 316.320489 | 7073900 |
| 316.320714 | 16065644 |
| 316.321274 | 166618220 |
| 316.322108 | 6202476 |
| 317.324847 | 22824056 |
| 329.229623 | 7806215 |
| 329.230195 | 56255751 |
| 347.137344 | 8457690 |
| 347.138654 | 416654810 |
| 348.141525 | 7857638 |
| 348.142210 | 74393062 |
| 349.134805 | 4886001 |
| 349.135114 | 12191217 |
| 349.135801 | 130786801 |
| 349.136452 | 10372593 |

| m/z | I |
|---|---|
| 350.139334 | 12670460 |
| 361.153769 | 7591543 |
| 361.154472 | 74835575 |
| 362.157914 | 7017090 |
| 363.151697 | 15726220 |
| 369.297993 | 42346190 |
| 401.288048 | 16173070 |
| 419.193623 | 4992182 |
| 419.194636 | 9966774 |
| 419.196155 | 486844598 |
| 419.197494 | 17504438 |
| 419.198034 | 9185462 |
| 419.198553 | 5664950 |
| 419.277439 | 11339959 |
| 420.198771 | 8337599 |
| 420.199756 | 106211519 |
| 421.193435 | 145434824 |
| 421.203375 | 5278921 |
| 422.197052 | 28166354 |
| 433.211063 | 4860215 |
| 433.212128 | 57485623 |
| 434.215756 | 7911744 |
| 435.191626 | 14555465 |
| 435.209387 | 10654025 |
| 437.194109 | 8227163 |
| 463.303715 | 46934601 |
| 464.307214 | 6387282 |
| 473.345599 | 24029862 |
| 479.228159 | 5229277 |
| 479.229347 | 51538653 |
| 491.253834 | 412527438 |
| 491.255679 | 14646094 |
| 491.256409 | 7539534 |
| 491.257137 | 4791118 |
| 492.257416 | 113257303 |
| 493.251011 | 134064993 |
| 493.260918 | 5084513 |
| 494.254686 | 29535082 |
| 507.328562 | 8821733 |
| 507.329867 | 92941285 |
| 508.333514 | 18443247 |
| 523.255595 | 86584441 |
| 524.255489 | 5932162 |
| 524.259229 | 7820418 |
| 545.403299 | 15101246 |
| 551.354394 | 7757169 |
| 551.356106 | 101985649 |
| 551.357715 | 8326513 |
| 552.359645 | 20008313 |
| 563.309889 | 8531410 |
| 563.311667 | 97168850 |
| 563.313422 | 7089618 |
| 564.315373 | 19103194 |
| 565.308942 | 18492898 |
| 567.280257 | 8039921 |
| 567.281863 | 84356593 |
| 568.281877 | 4872697 |
| 568.285542 | 8664569 |
| 595.380383 | 7900853 |
| 595.382299 | 83766965 |
| 595.384280 | 5840565 |

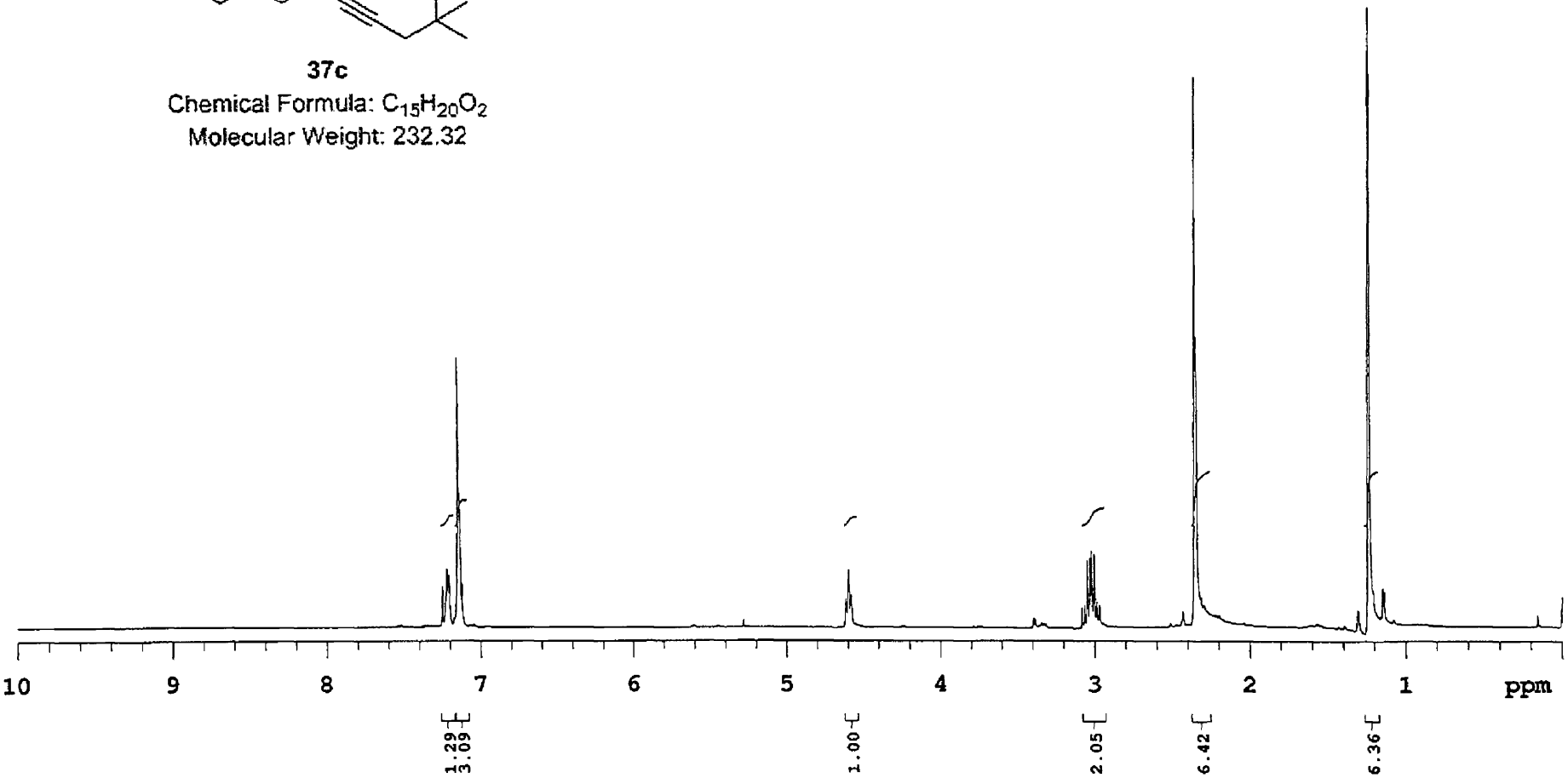
| m/z | I |
|---|---|
| 596.385997 | 14659259 |
| 611.306312 | 5234448 |
| 611.308268 | 33771280 |
| 635.369585 | 6641535 |
| 639.406686 | 6123407 |
| 639.408875 | 43708303 |
| 640.412075 | 5909395 |
| 655.334732 | 10778568 |
| 683.435192 | 10418201 |
| 685.430671 | 6238238 |
| 685.431959 | 9826334 |
| 685.435794 | 312782878 |
| 685.439777 | 7589918 |
| 685.441269 | 4939806 |
| 686.437131 | 10661920 |
| 686.439507 | 129249312 |
| 686.442130 | 9170976 |
| 687.443451 | 10655779 |




**37c**

Chemical Formula: $C_{15}H_{20}O_2$

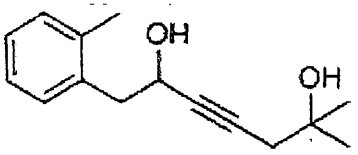
Molecular Weight: 232.32




| | | | | |
|---|---|---|---|---|
| PULSE SEQUENCE<br>Relax. delay 1.000 sec<br>Pulse 14.8 degrees<br>Acq. time 1.998 sec<br>Width 6402.0 Hz<br>2 repetitions | OBSERVE H1, 399.8398926 | DATA PROCESSING<br>Line broadening 1.0 Hz<br>FT size 32768<br>Total time 1 minute | | YC-187 pure pdt;<br>mono-methyl-sub.<br>alkynediol with<br>phenylpropionaldehyde to<br>form tricyclic<br>isochromenes; cdcl3;<br>7/20/2014<br>Temp#0.CDCl3.293.1.K |

YC-168 pure; mono-methyl-sub. diol cdcl3; 7/17/2014

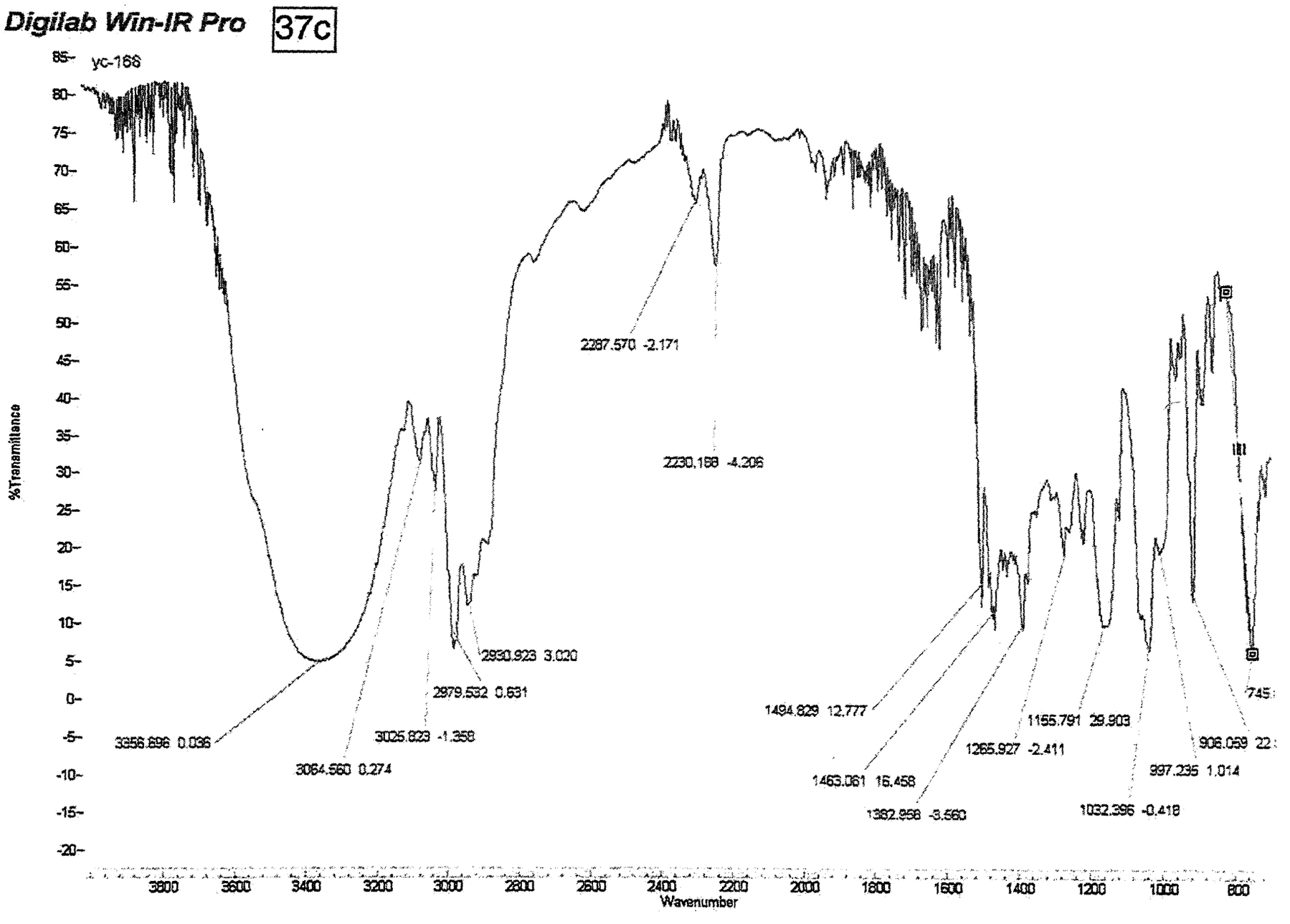
Sample Name:
yc-168




**37c**

Chemical Formula: $C_{15}H_{20}O_2$

Molecular Weight: 232.32


Digilab Win-IR Pro
37c
yc-168
%Transmittance
Wavenumber
3856.896 0.036
3064.560 0.274
3025.829 -1.358
2979.532 0.631
2930.923 3.020
2287.570 -2.171
2230.188 -4.206
1494.829 12.777
1463.061 16.458
1382.958 -3.560
1265.927 -2.411
1155.791 29.903
1032.396 -0.418
997.235 1.014
906.059 22
745

# Mass Spectrum List Report

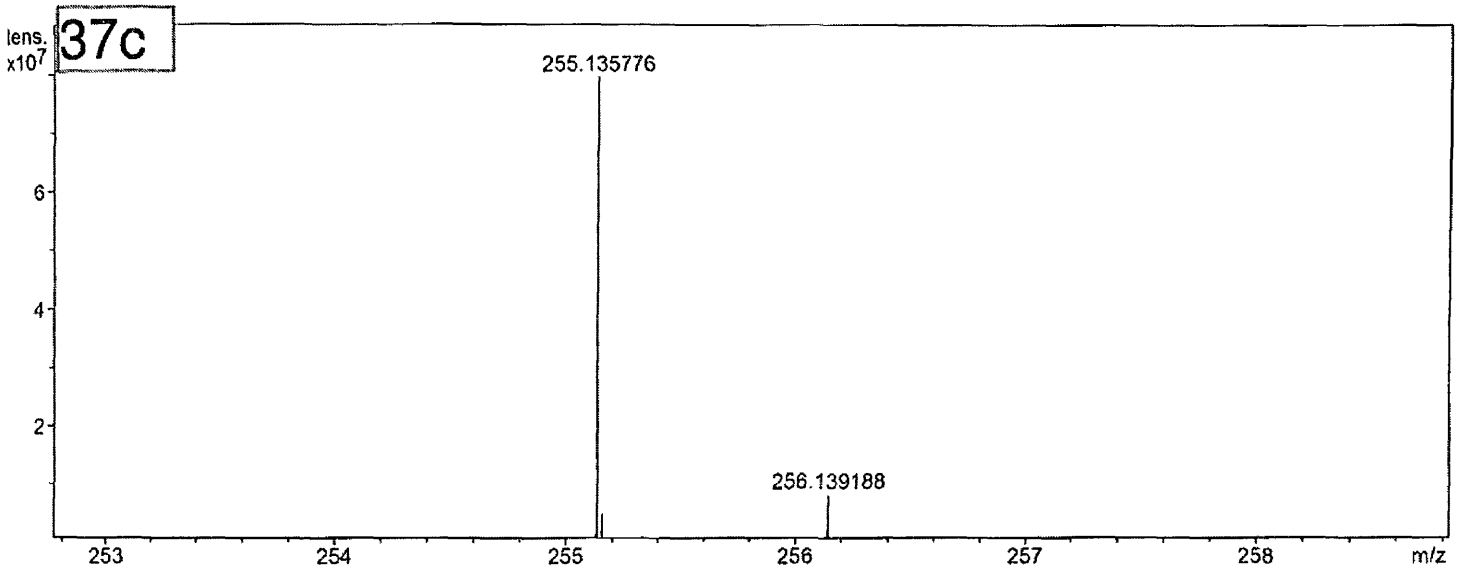


**Analysis Info**

| | | | |
|---|---|---|---|
| Analysis Name | YC-168_pos_000001.d | Acquisition Date | 7/22/2014 3:55:59 PM |
| Method | XMASS_Method | Operator | FTMS_USER |
| Sample Name: | YC-168_pos | Instrument | apex-Qe |
| | YC-168_pos: in 1:1 THF:MeOH w/ NaCl.. | | |

**Acquisition Parameter**

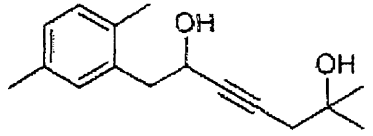
**Sample: YC-168**
**Exact Mass of = (C15H20O2)Na+ : 255.135551u**
**Observed Mass = 255.135776u**
**Difference = < 1.0 ppm**




| m/z | I |
|---|---|
| 175.253696 | 5785345 |
| 175.670086 | 15492313 |
| 220.086356 | 16995741 |
| 255.135776 | 79430203 |
| 255.136126 | 6510139 |
| 255.156988 | 4980027 |
| 256.139188 | 8248898 |
| 288.289562 | 12708706 |
| 288.289985 | 104096610 |
| 289.293422 | 13274989 |
| 316.321346 | 98280600 |
| 317.324838 | 15402148 |
| 327.193348 | 252093718 |
| 328.196222 | 4995361 |
| 328.196843 | 44401953 |
| 329.229698 | 8274221 |
| 329.230210 | 86074669 |
| 330.233670 | 8824121 |
| 332.316404 | 5794641 |
| 341.209151 | 47343030 |
| 342.212607 | 6903233 |

| m/z | I |
|---|---|
| 346.157401 | 7072237 |
| 383.277424 | 11298667 |
| 385.235544 | 10633086 |
| 399.237993 | 4818944 |
| 399.246042 | 4329472 |
| 399.246462 | 5754880 |
| 399.247738 | 53012480 |
| 399.248178 | 42096640 |
| 399.249253 | 25282560 |
| 399.250540 | 754362368 |
| 399.251433 | 53585920 |
| 399.251909 | 24430592 |
| 399.252380 | 13813760 |
| 399.252839 | 9553920 |
| 399.253300 | 6985728 |
| 399.253752 | 5216256 |
| 400.251652 | 14608393 |
| 400.252930 | 5265417 |
| 400.254191 | 123185161 |
| 400.254939 | 12163081 |
| 400.255432 | 5773321 |
| 401.255377 | 5797906 |
| 401.257930 | 14839826 |
| 401.285295 | 6243346 |
| 401.287952 | 36259858 |
| 402.291323 | 9652251 |
| 413.263984 | 8943740 |
| 413.266707 | 46966908 |
| 414.270247 | 7381125 |
| 415.246145 | 11122830 |
| 425.288043 | 8458468 |
| 435.345229 | 5716280 |
| 443.277522 | 12114297 |
| 455.335089 | 5950939 |
| 457.293191 | 21076459 |
| 458.296561 | 4317683 |
| 463.303821 | 11395612 |
| 468.309241 | 13027908 |
| 471.304456 | 14445148 |
| 471.305061 | 9149020 |
| 471.305911 | 15968860 |
| 471.306435 | 25553500 |
| 471.308248 | 843623004 |
| 471.311441 | 8419932 |
| 471.312083 | 5929564 |
| 471.312749 | 4488796 |
| 472.308126 | 7332452 |
| 472.309935 | 5375588 |
| 472.310581 | 14166628 |
| 472.311825 | 244492900 |
| 472.312990 | 20933220 |
| 472.313641 | 9652836 |
| 473.315553 | 26634860 |
| 473.345572 | 31640172 |
| 474.349100 | 7078516 |
| 479.229502 | 11791004 |
| 507.330077 | 20347772 |
| 508.333494 | 4864899 |
| 519.309006 | 6030298 |
| 523.255816 | 18758649 |
| 533.324683 | 6450247 |

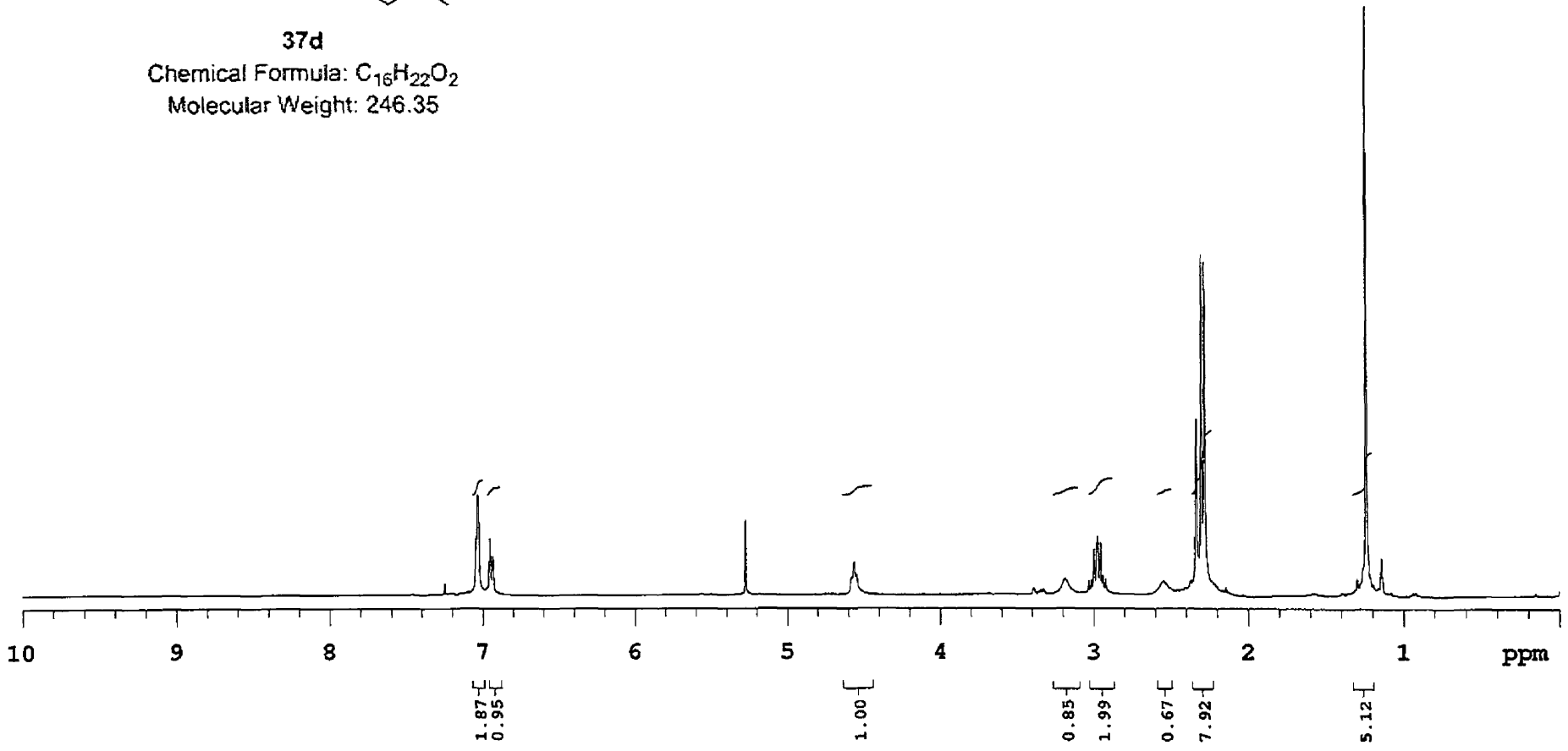
| m/z | I |
|---|---|
| 540.366906 | 4379772 |
| 543.364697 | 7802003 |
| 543.366371 | 88583315 |
| 543.368007 | 5975187 |
| 544.369842 | 24153243 |
| 545.403336 | 7226531 |
| 551.356387 | 29904079 |
| 552.359759 | 6827223 |
| 567.282117 | 23006533 |
| 587.429258 | 4385236 |
| 595.382668 | 19754507 |
| 596.386109 | 5826065 |
| 611.308429 | 9289331 |
| 639.409107 | 9715477 |
| 655.334807 | 4482911 |
| 683.435357 | 4595636 |
| 685.436775 | 33107895 |
| 686.440286 | 10706873 |




**37d**

Chemical Formula: $C_{16}H_{22}O_2$

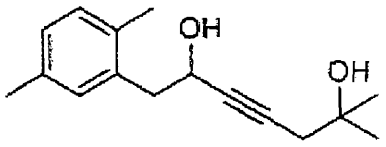
Molecular Weight: 246.35




| | | | | |
|---|---|---|---|---|
| PULSE SEQUENCE<br>Relax. delay 1.000 sec<br>Pulse 14.8 degrees<br>Acq. time 1.998 sec<br>Width 6402.0 Hz<br>8 repetitions | OBSERVE H1, 400.1766864 | DATA PROCESSING<br>FT size 32768<br>Total time 1 minute | | YC-167 pure 2,5-dimethyl sub. diol; cdcl3; 5/19/2014<br>Solvent: cdcl3<br>Ambient temperature<br>Operator: rjhink<br>File: YC-167-h-2 |

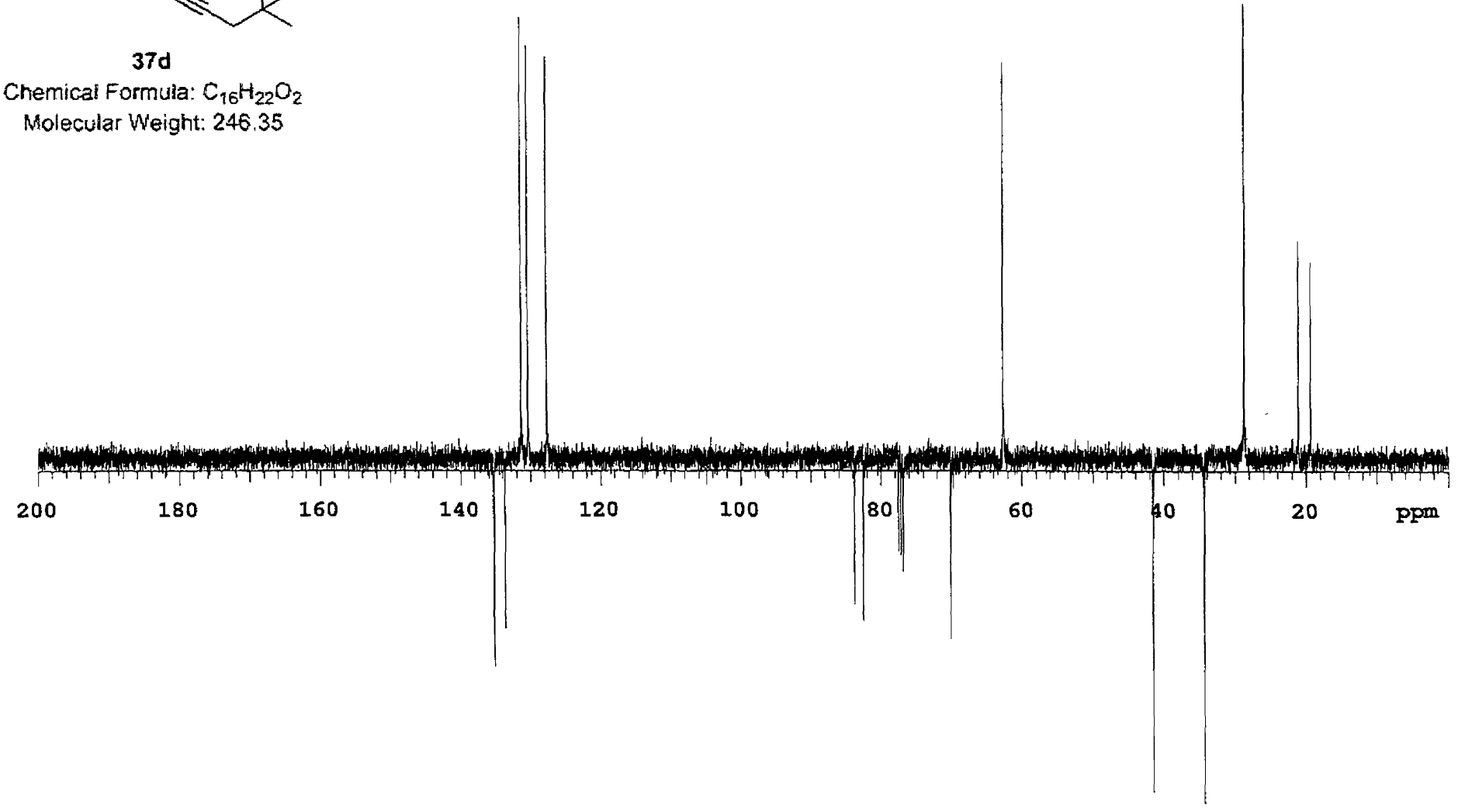
YC-167 pure 2,5-dimethyl sub. diol; cdcl3; 5/19/2014

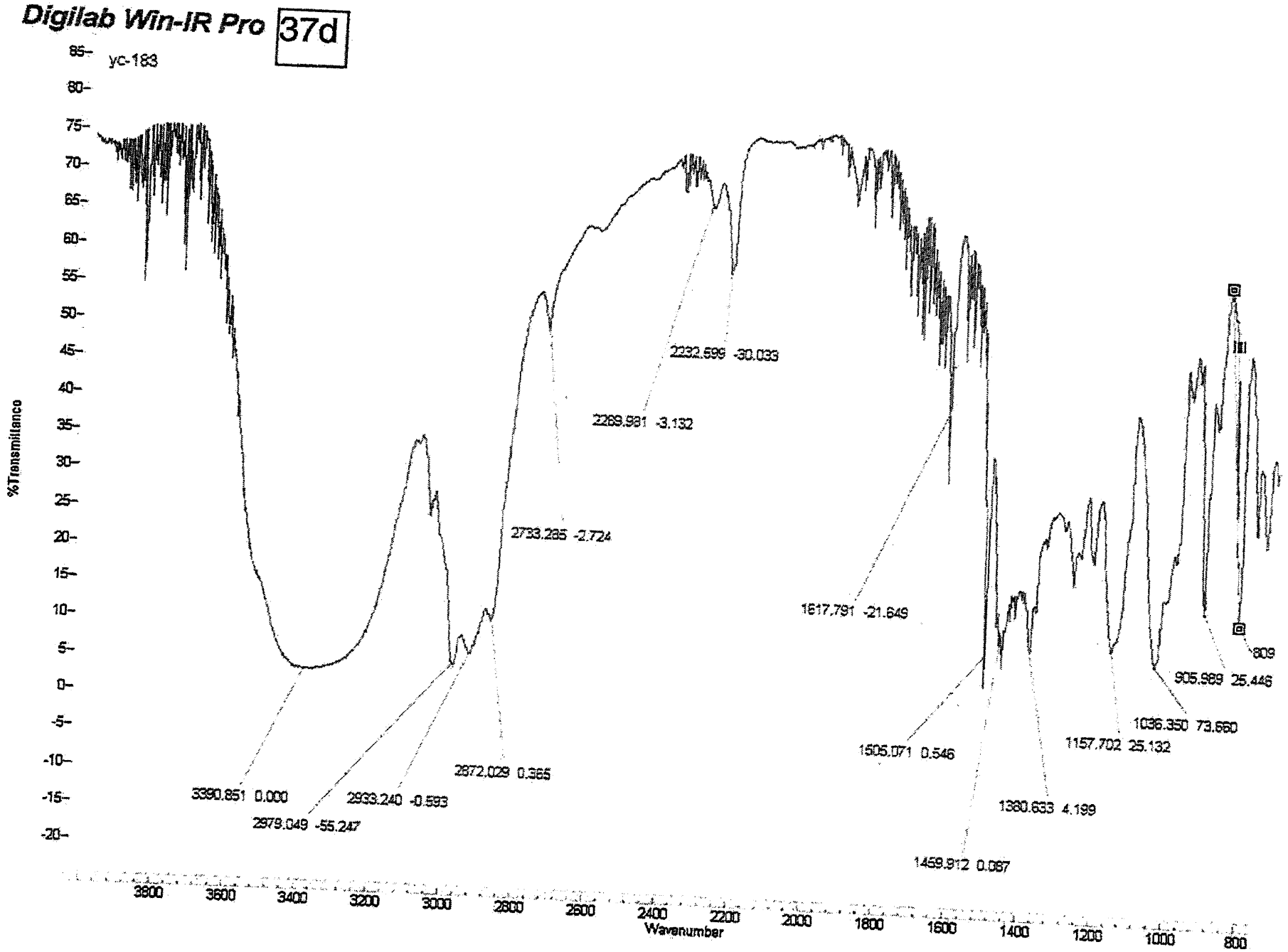
Sample Name:
yc-167




**37d**

Chemical Formula: $C_{16}H_{22}O_2$
Molecular Weight: 246.35




Digilab Win-IR Pro
37d
yc-183
%Transmittance
Wavenumber
3390.851 0.000
2979.049 -55.247
2933.240 -0.593
2872.029 0.365
2733.285 -2.724
2269.981 -3.132
2232.699 -30.033
1617.791 -21.649
1505.071 0.546
1459.912 0.067
1380.633 4.199
1157.702 25.132
1036.350 73.660
905.989 25.446
809

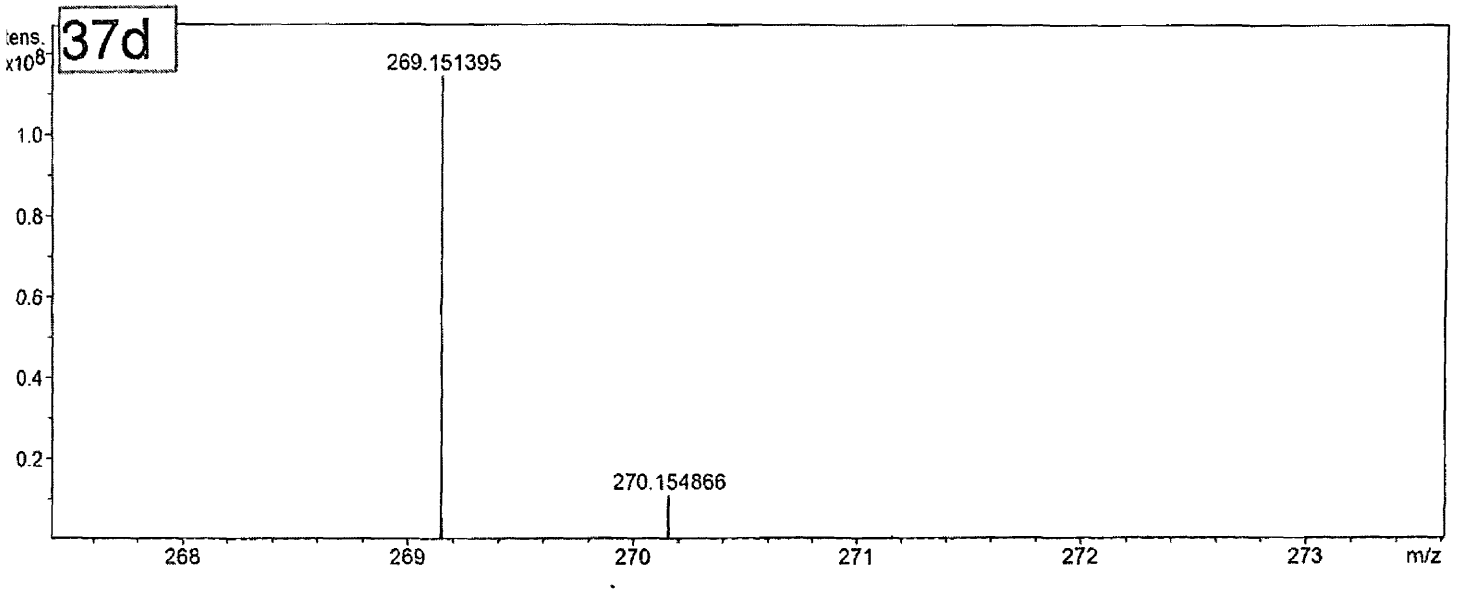
# Mass Spectrum List Report

**Analysis Info**

| | | | |
|---|---|---|---|
| Analysis Name | YC-183_pos_000001.d | Acquisition Date | 7/22/2014 4:00:34 PM |
| Method | XMASS_Method | Operator | FTMS_USER |
| Sample Name: | YC-183_pos | Instrument | apex-Qe |
| | YC-183_pos: in 1:1 THF:MeOH w/ NaCl.. | | |

**Acquisition Parameter**

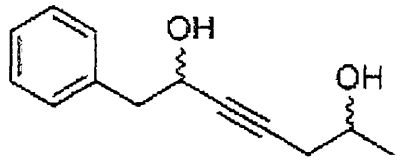
**Sample: YC-183**
**Exact Mass of = (C16H22O2)Na+ : 269.151201u**
**Observed Mass = 269.151395u**
**Difference = < 1.0 ppm**




| m/z | I |
|---|---|
| 169.806188 | 6695828 |
| 170.174775 | 19924536 |
| 208.397999 | 18350967 |
| 269.151012 | 16237206 |
| 269.151395 | 114057878 |
| 269.151777 | 9878166 |
| 270.154866 | 10972831 |
| 288.289942 | 106488664 |
| 288.290354 | 10662744 |
| 289.293386 | 12462947 |
| 306.233465 | 17323051 |
| 316.320480 | 5631147 |
| 316.320728 | 10953899 |
| 316.321291 | 117793963 |
| 316.321819 | 10312875 |
| 317.324848 | 15342775 |
| 329.229556 | 9260372 |
| 329.230139 | 87500116 |
| 329.230707 | 7572820 |
| 330.233646 | 7915873 |
| 334.310954 | 5532567 |

| m/z | I |
|---|---|
| 338.209556 | 6392267 |
| 341.206903 | 5070324 |
| 341.207244 | 7495156 |
| 341.207590 | 12453364 |
| 341.207882 | 14898676 |
| 341.208230 | 34219508 |
| 341.208908 | 590259700 |
| 341.209526 | 51930612 |
| 341.209872 | 21964276 |
| 341.210214 | 12346868 |
| 341.210555 | 7638516 |
| 341.210894 | 5436916 |
| 342.211734 | 11101697 |
| 342.212396 | 119465473 |
| 342.213010 | 10540545 |
| 343.215945 | 5900815 |
| 355.224032 | 6440623 |
| 355.224743 | 57697967 |
| 356.228228 | 6237884 |
| 369.298083 | 10125161 |
| 383.277443 | 5978141 |
| 399.251184 | 5704931 |
| 401.287741 | 137832699 |
| 401.288515 | 13236475 |
| 401.288992 | 5402875 |
| 402.291258 | 20478215 |
| 413.263533 | 5486984 |
| 413.264035 | 8067464 |
| 413.264521 | 14051720 |
| 413.264970 | 17983880 |
| 413.265523 | 39528840 |
| 413.266438 | 636004744 |
| 413.267366 | 48441736 |
| 413.267896 | 20834696 |
| 413.268402 | 11831688 |
| 413.268898 | 7526792 |
| 413.269397 | 5061000 |
| 414.268528 | 5929363 |
| 414.269010 | 13781395 |
| 414.269942 | 162441619 |
| 414.271403 | 5216659 |
| 415.273612 | 11882911 |
| 419.277467 | 6439372 |
| 425.288028 | 8653326 |
| 427.281354 | 7354915 |
| 427.282360 | 84011555 |
| 428.285882 | 15100462 |
| 429.261866 | 12112440 |
| 441.354580 | 7871156 |
| 441.355593 | 81455796 |
| 442.359101 | 13017790 |
| 463.303778 | 20142970 |
| 473.344208 | 6532041 |
| 473.345460 | 59321289 |
| 474.349067 | 9810896 |
| 479.229441 | 14191603 |
| 485.323934 | 699182107 |
| 485.326382 | 12569628 |
| 485.327054 | 7834652 |
| 485.327742 | 4978716 |
| 486.327471 | 226536482 |

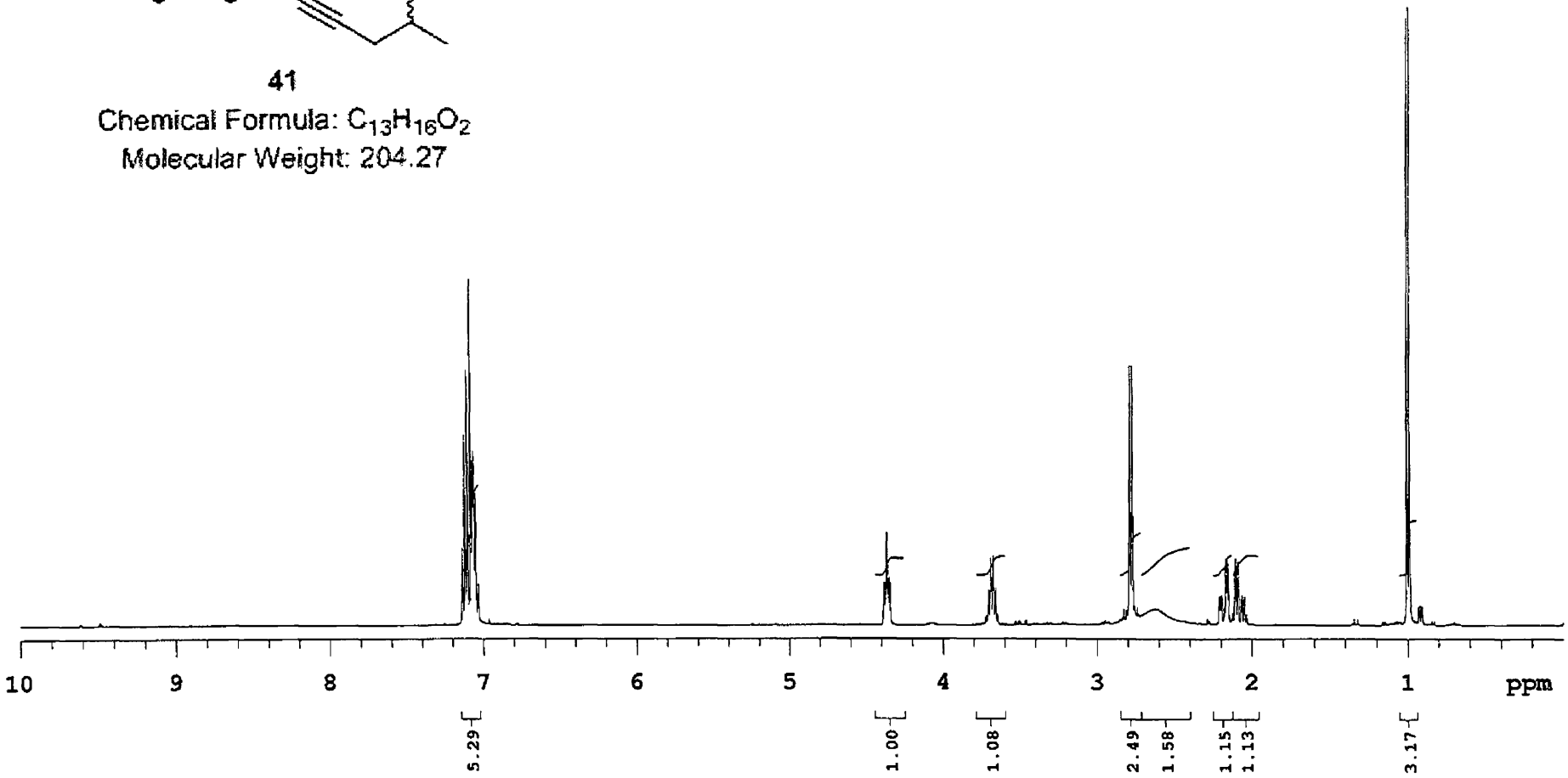
| m/z | I |
|---|---|
| 487.331188 | 26422312 |
| 507.329980 | 40340632 |
| 508.333502 | 6890653 |
| 513.413482 | 5797046 |
| 523.255772 | 20532449 |
| 545.403267 | 16788788 |
| 551.356271 | 41422152 |
| 552.359697 | 6858059 |
| 557.380257 | 6327643 |
| 557.381982 | 62745947 |
| 558.385547 | 12406110 |
| 567.282060 | 23932280 |
| 595.382515 | 26521034 |
| 596.385941 | 4966861 |
| 611.308350 | 7904762 |
| 639.408997 | 9752147 |
| 685.436543 | 36351712 |
| 686.440125 | 9025251 |




41

Chemical Formula: $C_{13}H_{16}O_2$

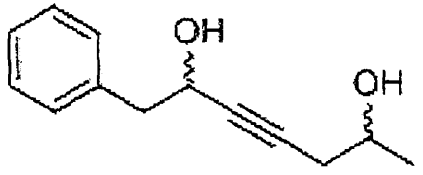
Molecular Weight: 204.27




| | | | | |
|---|---|---|---|---|
| PULSE SEQUENCE<br>Relax. delay 1.000 sec<br>Pulse 45.0 degrees<br>Acq. time 3.408 sec<br>Width 4807.7 Hz<br>4 repetitions | OBSERVE H1, 399.8399674 | DATA PROCESSING<br>FT size 32768<br>Total time 1 minute | | CPN-40 propylene oxide with alkyne monoalcohol to form diol<br>Solvent: cdcl3<br>Ambient temperature<br>Operator: rjhink<br>File: cpn-40-h-2 |

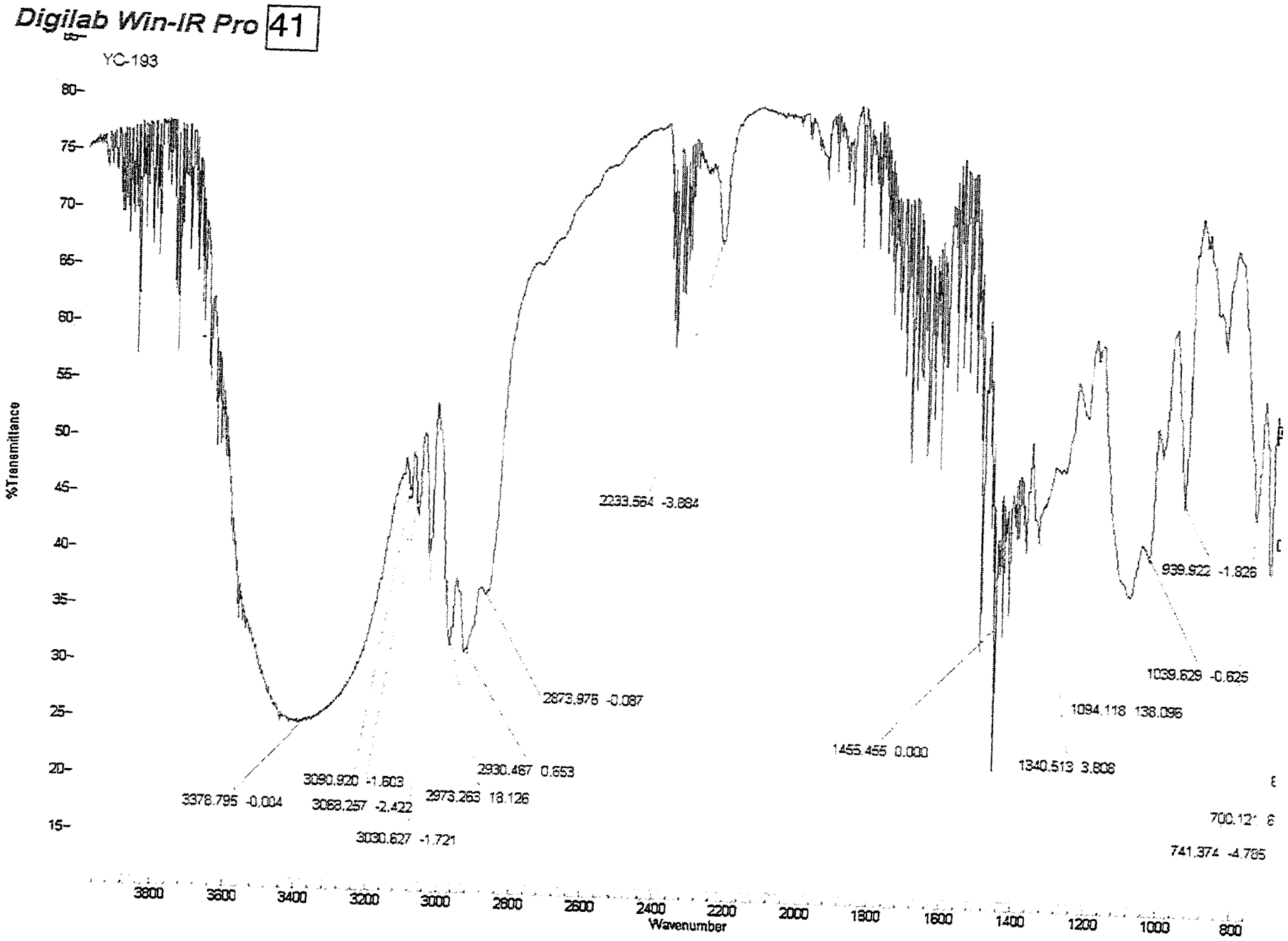
CPN-40 propylene oxide with alkyne monoalcohol to form diol(racemic)

Sample Name:
cpn-40




**41**

Chemical Formula: $C_{13}H_{16}O_2$
Molecular Weight: 204.27


Digilab Win-IR Pro 41
YC-193
%Transmittance
Wavenumber
3378.795 -0.004
3090.920 -1.603
3068.257 -2.422
3030.627 -1.721
2973.263 18.126
2930.467 0.653
2873.975 -0.087
2233.564 -3.884
1455.455 0.000
1340.513 3.808
1094.118 138.096
1039.629 -0.625
939.922 -1.826
741.374 -4.785

# Mass Spectrum List Report

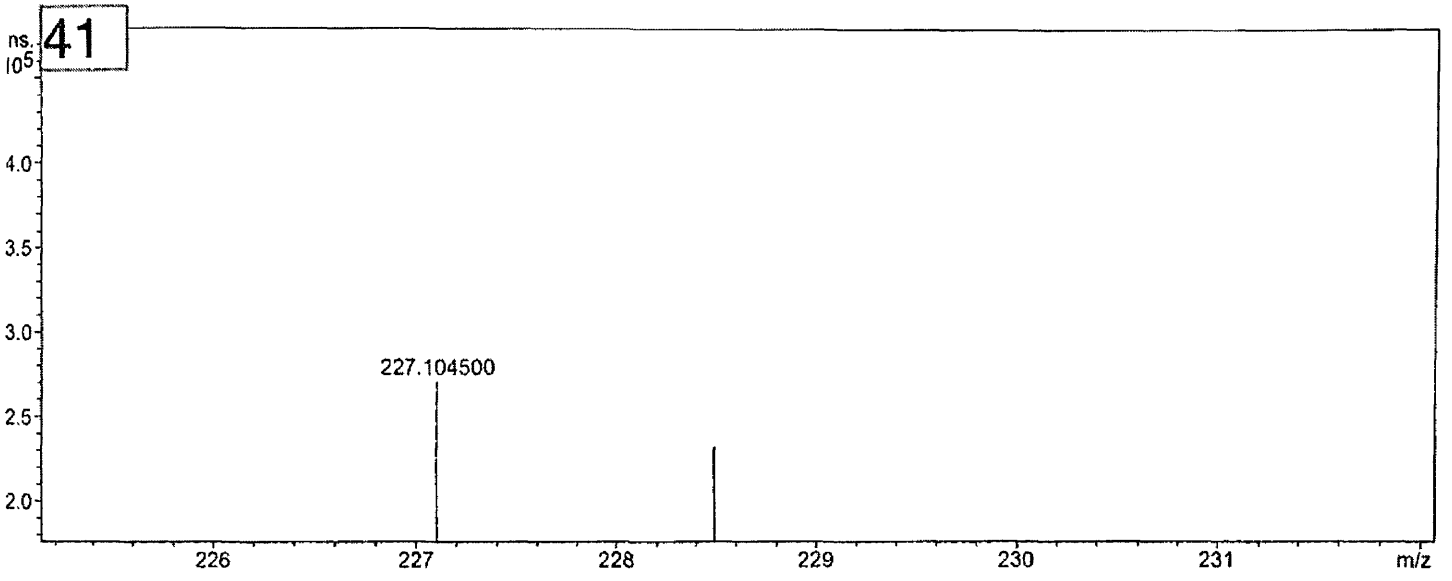


**Analysis Info**

| | | | |
|---|---|---|---|
| Analysis Name | YC-193_pos_000001.d | Acquisition Date | 7/22/2014 4:33:48 PM |
| Method | XMASS_Method | Operator | FTMS_USER |
| Sample Name: | YC-193_pos | Instrument | apex-Qe |
| | YC-193_pos: in 1:1 THF:MeOH w/ NaCl.. | | |

**Acquisition Parameter**

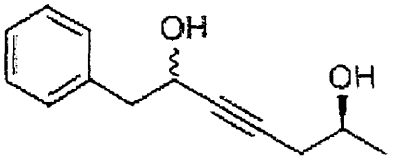
**Sample: YC-193**
**Exact Mass of = (C13H16O2)Na+ : 227.104251u**
**Observed Mass = 227.104500u**
**Difference = 1.1 ppm**




| m/z | I |
|---|---|
| 248.809634 | 4213230 |
| 273.285160 | 13912797 |
| 285.145333 | 16274794 |
| 285.146206 | 151642986 |
| 285.146641 | 12919658 |
| 285.146884 | 6087530 |
| 286.149668 | 49836918 |
| 286.150094 | 4501366 |
| 288.288946 | 14042513 |
| 288.289813 | 139633553 |
| 288.290246 | 14734225 |
| 288.290472 | 6819729 |
| 288.290727 | 3824017 |
| 289.292346 | 4278942 |
| 289.293319 | 13587358 |
| 299.162040 | 25052190 |
| 301.551056 | 13921341 |
| 304.284931 | 8040545 |
| 313.177763 | 12944601 |
| 316.320030 | 5318915 |
| 316.320313 | 8629507 |

| m/z | I |
|---|---|
| 316.320626 | 13954307 |
| 316.321161 | 207070467 |
| 316.321663 | 19412227 |
| 316.321977 | 8455427 |
| 316.322266 | 4677891 |
| 317.324157 | 7073040 |
| 317.324661 | 40441104 |
| 332.316260 | 4300758 |
| 343.186070 | 4120158 |
| 343.186415 | 6223454 |
| 343.186754 | 10561118 |
| 343.187080 | 13317726 |
| 343.187425 | 33629790 |
| 343.188098 | 485271134 |
| 343.188725 | 40691294 |
| 343.189080 | 17827422 |
| 343.189423 | 9889374 |
| 343.189765 | 6174302 |
| 343.190108 | 4177502 |
| 344.191584 | 86959722 |
| 345.195069 | 6474358 |
| 355.282238 | 15048426 |
| 357.202369 | 11601663 |
| 357.202710 | 16852735 |
| 357.203734 | 489203455 |
| 358.206184 | 4430602 |
| 358.206531 | 10524426 |
| 358.207212 | 97019658 |
| 359.210739 | 6464277 |
| 371.218856 | 6635407 |
| 371.219582 | 45672335 |
| 372.223073 | 7635864 |
| 373.197202 | 3637153 |
| 373.197579 | 6559649 |
| 373.198005 | 13186977 |
| 373.198720 | 152971169 |
| 373.199893 | 4923297 |
| 374.201618 | 4177835 |
| 374.202273 | 24340395 |
| 385.234530 | 5136398 |
| 385.235311 | 30222350 |
| 386.238726 | 5535767 |
| 388.542976 | 5866538 |
| 401.230293 | 5663888 |
| 415.244978 | 4468984 |
| 415.245896 | 32098552 |
| 416.249358 | 6523135 |
| 419.277263 | 13670676 |
| 425.287849 | 9736509 |
| 429.261640 | 13257047 |
| 463.303493 | 36112944 |
| 464.306923 | 7821879 |
| 477.261701 | 3760778 |
| 479.229212 | 23816854 |
| 480.232629 | 3550877 |
| 507.328290 | 3707730 |
| 507.329671 | 53701458 |
| 507.331033 | 4365138 |
| 508.333160 | 12118872 |
| 523.255458 | 30682047 |
| 524.258887 | 4970438 |

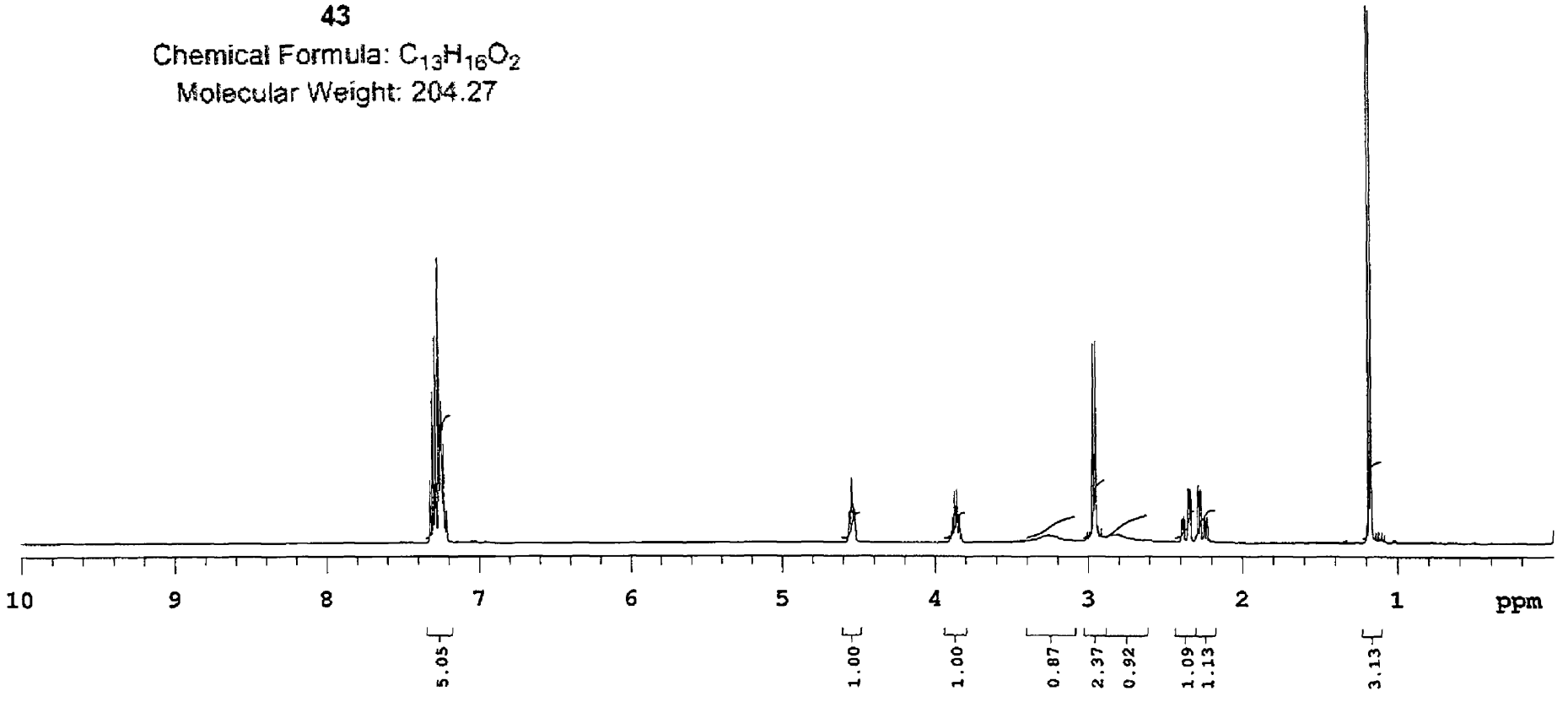
| m/z | I |
|---|---|
| 551.354444 | 4902018 |
| 551.355944 | 54422658 |
| 552.359370 | 11742345 |
| 567.281727 | 28585201 |
| 568.285168 | 5342456 |
| 595.382197 | 32443826 |
| 596.385661 | 7527865 |
| 605.490150 | 3581430 |
| 611.307956 | 12172828 |
| 639.408625 | 15335109 |
| 640.411943 | 4719306 |
| 650.689638 | 3671805 |
| 655.334375 | 5472018 |
| 659.334850 | 37302051 |
| 660.338439 | 12013351 |
| 683.434765 | 7092075 |
| 685.436217 | 30117743 |
| 686.439671 | 10616688 |




**43**

Chemical Formula: $C_{13}H_{16}O_2$

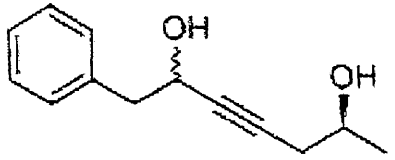
Molecular Weight: 204.27




| | | | | |
|---|---|---|---|---|
| PULSE SEQUENCE<br>Relax. delay 1.000 sec<br>Pulse 45.0 degrees<br>Acq. time 2.556 sec<br>Width 6410.3 Hz<br>4 repetitions | OBSERVE H1, 399.8398916 | DATA PROCESSING<br>FT size 32768<br>Total time 1 minute | | YC-193 pure; diol form alkyne monoalcohol and (S)-(-)-propylene oxide; cdcl3; 6/22/2014<br>106<br>Solvent: cdcl3<br>Ambient temperature<br>Operator: rjhink |

YC-193 pure; diol form alkyne monoalcohol and (S)-(-)-propylene oxide; cdcl3; 6/22/2014

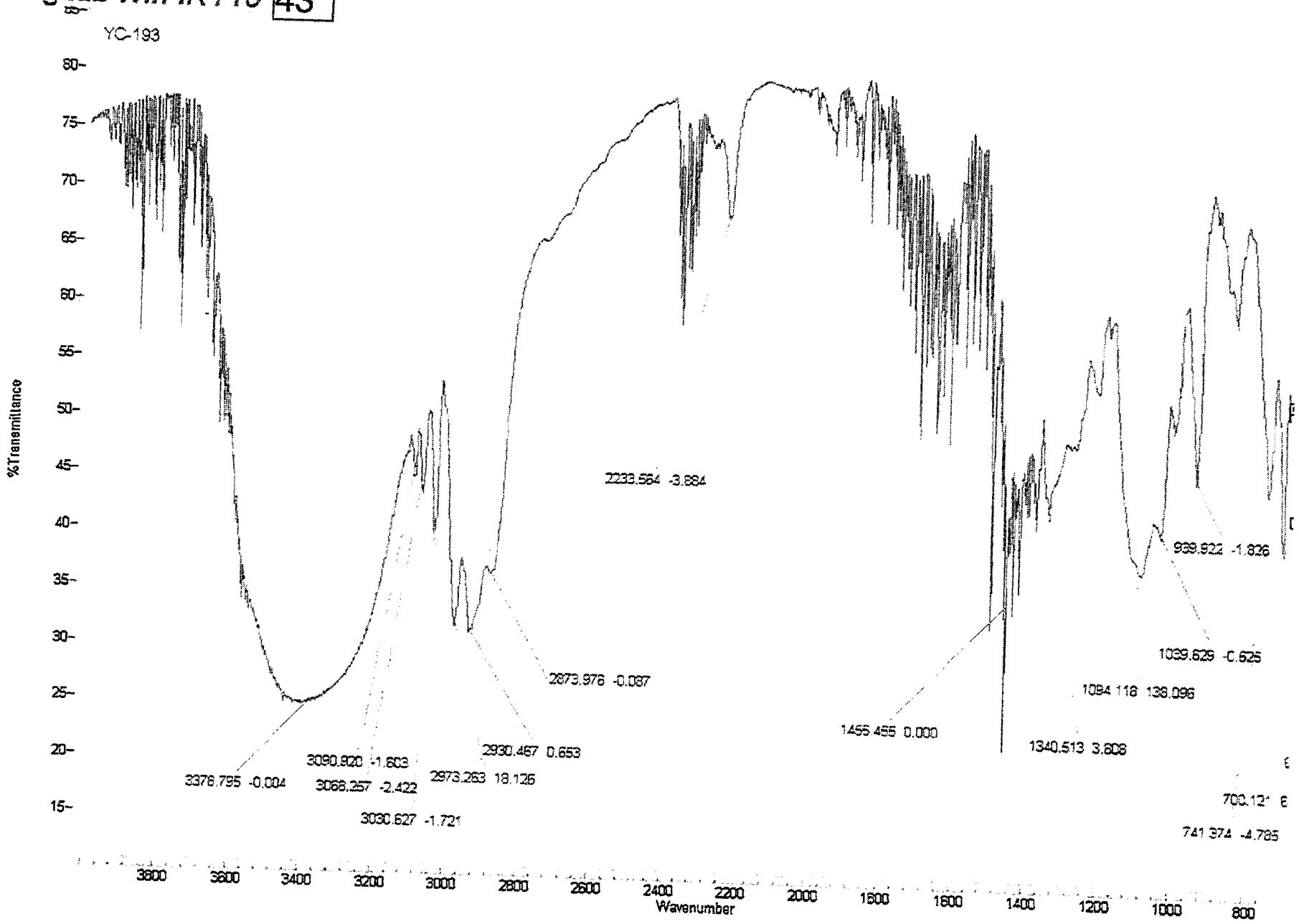
Sample Name:




**43**

Chemical Formula: $C_{13}H_{16}O_2$

Molecular Weight: 204.27


Digilab Win-IR Pro 43
YC-193
%Transmittance
Wavenumber
3378.795 -0.004
3090.920 -1.603
3066.257 -2.422
3030.627 -1.721
2973.263 18.126
2930.467 0.653
2873.976 -0.087
2233.554 -3.884
1455.455 0.000
1340.513 3.808
1094.116 136.096
1039.629 -0.625
939.922 -1.826
741.374 -4.785

# Mass Spectrum List Report

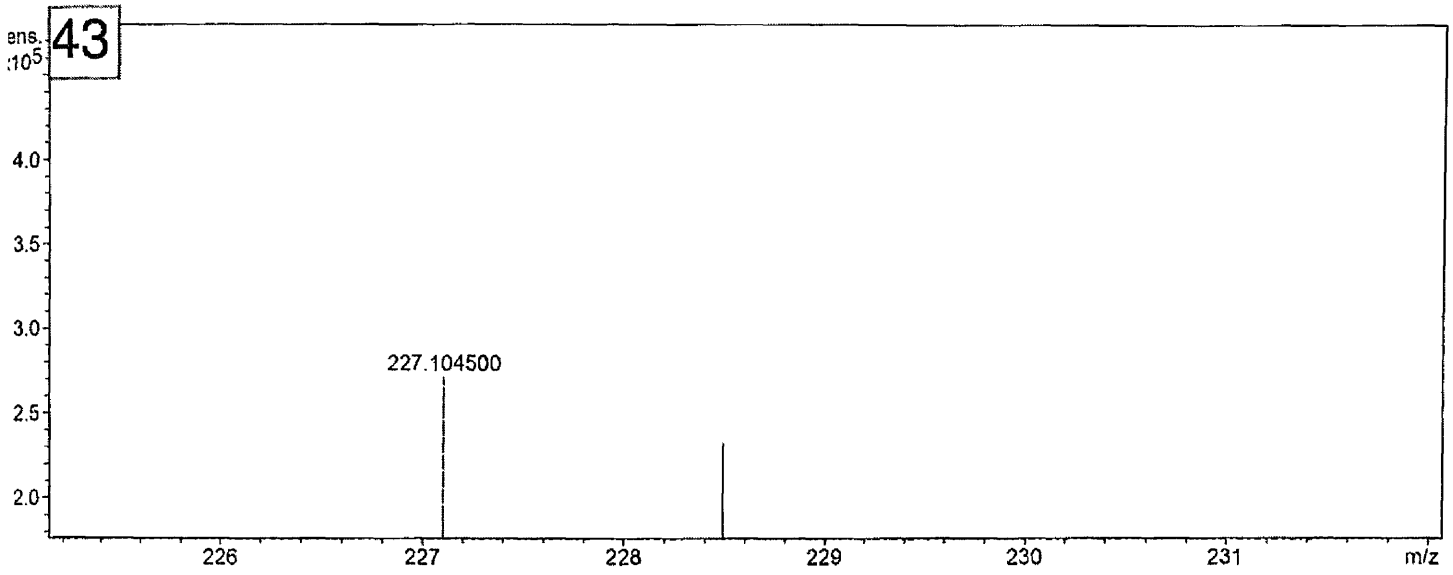


**Analysis Info**

| | | | |
|---|---|---|---|
| Analysis Name | YC-193_pos_000001.d | Acquisition Date | 7/22/2014 4:33:48 PM |
| Method | XMASS_Method | Operator | FTMS_USER |
| Sample Name: | YC-193_pos | Instrument | apex-Qe |
| | YC-193_pos: in 1:1 THF:MeOH w/ NaCl.. | | |

**Acquisition Parameter**

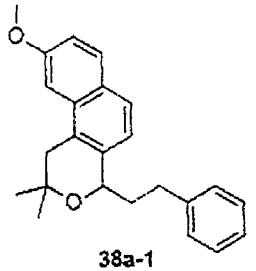
**Sample: YC-193**
**Exact Mass of = (C13H16O2)Na+ : 227.104251u**
**Observed Mass = 227.104500u**
**Difference = 1.1 ppm**




| m/z | I |
|---|---|
| 248.809634 | 4213230 |
| 273.285160 | 13912797 |
| 285.145333 | 16274794 |
| 285.146206 | 151642986 |
| 285.146641 | 12919658 |
| 285.146884 | 6087530 |
| 286.149668 | 49836918 |
| 286.150094 | 4501366 |
| 288.288946 | 14042513 |
| 288.289813 | 139633553 |
| 288.290246 | 14734225 |
| 288.290472 | 6819729 |
| 288.290727 | 3824017 |
| 289.292346 | 4278942 |
| 289.293319 | 13587358 |
| 299.162040 | 25052190 |
| 301.551056 | 13921341 |
| 304.284931 | 8040545 |
| 313.177763 | 12944601 |
| 316.320030 | 5318915 |
| 316.320313 | 8629507 |

| m/z | I |
|---|---|
| 316.320626 | 13954307 |
| 316.321161 | 207070467 |
| 316.321663 | 19412227 |
| 316.321977 | 8455427 |
| 316.322266 | 4677891 |
| 317.324157 | 7073040 |
| 317.324661 | 40441104 |
| 332.316260 | 4300758 |
| 343.186070 | 4120158 |
| 343.186415 | 6223454 |
| 343.186754 | 10561118 |
| 343.187080 | 13317726 |
| 343.187425 | 33629790 |
| 343.188098 | 485271134 |
| 343.188725 | 40691294 |
| 343.189080 | 17827422 |
| 343.189423 | 9889374 |
| 343.189765 | 6174302 |
| 343.190108 | 4177502 |
| 344.191584 | 86959722 |
| 345.195069 | 6474358 |
| 355.282238 | 15048426 |
| 357.202369 | 11601663 |
| 357.202710 | 16852735 |
| 357.203734 | 489203455 |
| 358.206184 | 4430602 |
| 358.206531 | 10524426 |
| 358.207212 | 97019658 |
| 359.210739 | 6464277 |
| 371.218856 | 6635407 |
| 371.219582 | 45672335 |
| 372.223073 | 7635864 |
| 373.197202 | 3637153 |
| 373.197579 | 6559649 |
| 373.198005 | 13186977 |
| 373.198720 | 152971169 |
| 373.199893 | 4923297 |
| 374.201618 | 4177835 |
| 374.202273 | 24340395 |
| 385.234530 | 5136398 |
| 385.235311 | 30222350 |
| 386.238726 | 5535767 |
| 388.542976 | 5866538 |
| 401.230293 | 5663888 |
| 415.244978 | 4468984 |
| 415.245896 | 32098552 |
| 416.249358 | 6523135 |
| 419.277263 | 13670676 |
| 425.287849 | 9736509 |
| 429.261640 | 13257047 |
| 463.303493 | 36112944 |
| 464.306923 | 7821879 |
| 477.261701 | 3760778 |
| 479.229212 | 23816854 |
| 480.232629 | 3550877 |
| 507.328290 | 3707730 |
| 507.329671 | 53701458 |
| 507.331033 | 4365138 |
| 508.333160 | 12118872 |
| 523.255458 | 30682047 |
| 524.258887 | 4970438 |

| m/z | I |
|---|---|
| 551.354444 | 4902018 |
| 551.355944 | 54422658 |
| 552.359370 | 11742345 |
| 567.281727 | 28585201 |
| 568.285168 | 5342456 |
| 595.382197 | 32443826 |
| 596.385661 | 7527865 |
| 605.490150 | 3581430 |
| 611.307956 | 12172828 |
| 639.408625 | 15335109 |
| 640.411943 | 4719306 |
| 650.689638 | 3671805 |
| 655.334375 | 5472018 |
| 659.334850 | 37302051 |
| 660.338439 | 12013351 |
| 683.434765 | 7092075 |
| 685.436217 | 30117743 |
| 686.439671 | 10616688 |



**38a-1**

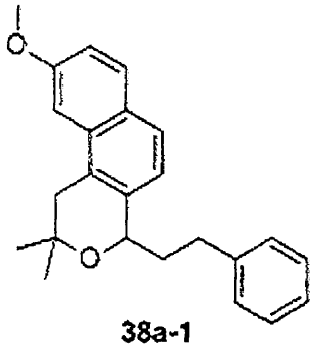
Chemical Formula: $C_{24}H_{26}O_2$

Molecular Weight: 346.47




| | | | | |
|---|---|---|---|---|
| PULSE SEQUENCE<br>Relax. delay 1.000 sec<br>Pulse 45.0 degrees<br>Acq. time 2.556 sec<br>Width 6410.3 Hz<br>8 repetitions | OBSERVE H1, 399.8398924 | DATA PROCESSING<br>FT size 32768<br>Total time 1 minute | | YC-148 pure pdt;<br>methoxy-sub. alkynediol with phenylpropionaldehyde to form tricyclic isochromenes; cdcl3;<br>7/19/2014<br>Sample8 0dCl3 293.1 K |

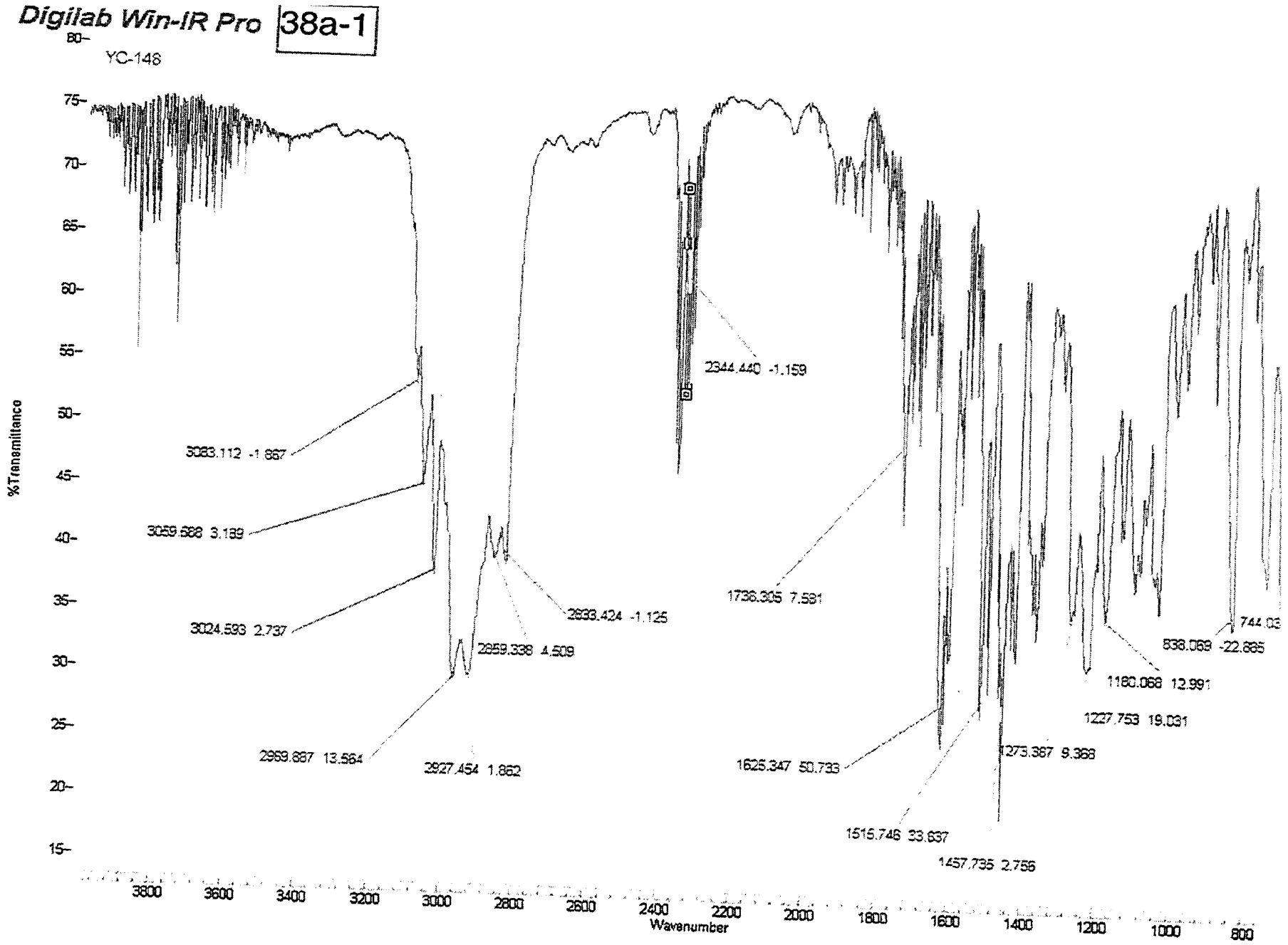
YC-148 pure pdt; methoxy-diol with phenylpropionaldehyde to form tricyclic isochromene; cdcl3; 6/8/2014



**38a-1**

Chemical Formula: $C_{24}H_{26}O_2$

Molecular Weight: 346.47


Digilab Win-IR Pro
38a-1
YC-148
%Transmittance
Wavenumber
3083.112 -1.867
3059.688 3.189
3024.593 2.737
2969.887 13.564
2927.454 1.862
2959.338 4.509
2933.424 -1.125
2344.440 -1.159
1736.305 7.581
1625.347 50.733
1515.746 33.637
1457.735 2.756
1373.387 9.368
1227.753 19.031
1180.068 12.991
838.069 -22.885
744.03

# Mass Spectrum List Report

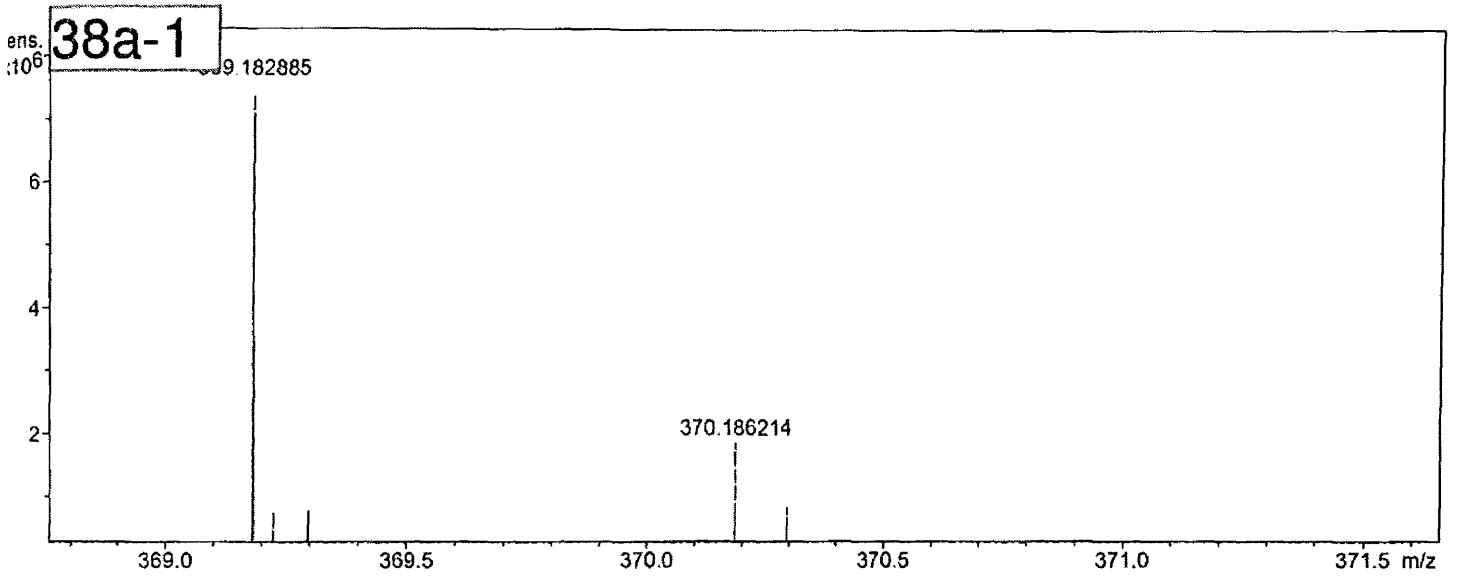


**Analysis Info**

| | | | |
|---|---|---|---|
| Analysis Name | YC-148_pos_000001.d | Acquisition Date | 7/22/2014 3:46:33 PM |
| Method | XMASS_Method | Operator | FTMS_USER |
| Sample Name: | YC-148_pos | Instrument | apex-Qe |
| | YC-148_pos: in 1:1 THF:MeOH w/ NaCl.. | | |

**Acquisition Parameter**

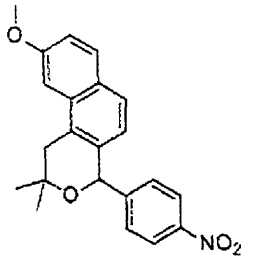
**Sample: YC-148**
**Exact Mass of = (C24H26O2)Na+ : 369.182501u**
**Observed Mass = 369.182885u**
**Difference = 1.0 ppm**




| m/z | I |
|---|---|
| 288.288883 | 11806682 |
| 288.289797 | 216114138 |
| 288.290231 | 20902874 |
| 288.290474 | 9724890 |
| 288.290726 | 5304282 |
| 288.290970 | 3346394 |
| 289.293294 | 16645097 |
| 304.284452 | 3480522 |
| 304.284882 | 17994954 |
| 316.320013 | 15123838 |
| 316.321080 | 202745214 |
| 317.323461 | 4242829 |
| 317.324063 | 4531597 |
| 317.324589 | 56657293 |
| 332.316177 | 36353634 |
| 333.319635 | 5422704 |
| 343.169618 | 12824302 |
| 345.184554 | 4118278 |
| 345.185192 | 30832390 |
| 346.188634 | 5783314 |
| 360.324056 | 5271462 |

| m/z | I |
|---|---|
| 360.347563 | 4596647 |
| 369.182885 | 7574516 |
| 372.347598 | 3371534 |
| 375.250989 | 4859940 |
| 383.141052 | 5813340 |
| 388.543424 | 4125823 |
| 393.297916 | 4577436 |
| 413.266508 | 67807496 |
| 413.267387 | 6011144 |
| 414.270006 | 13465869 |
| 419.276244 | 3490086 |
| 419.277177 | 27257126 |
| 420.280585 | 4759851 |
| 421.233041 | 10869040 |
| 425.287826 | 4254021 |
| 435.202959 | 4200823 |
| 435.344937 | 5970296 |
| 437.192724 | 5740930 |
| 437.193753 | 65137026 |
| 437.194806 | 4659586 |
| 438.197232 | 13560199 |
| 439.203677 | 13298061 |
| 441.296995 | 4809112 |
| 441.297890 | 42985880 |
| 442.301334 | 9404830 |
| 453.167840 | 8698334 |
| 455.313668 | 7737836 |
| 463.302211 | 4432418 |
| 463.303390 | 55994914 |
| 463.304545 | 4543010 |
| 464.306877 | 11102761 |
| 479.227877 | 3560099 |
| 479.229100 | 37415587 |
| 480.228786 | 3856044 |
| 480.232544 | 4819628 |
| 495.266304 | 34343744 |
| 496.269681 | 8248138 |
| 507.224108 | 3969984 |
| 507.328209 | 5663681 |
| 507.329575 | 74017729 |
| 507.330981 | 5217217 |
| 508.333110 | 17423308 |
| 523.253901 | 4177013 |
| 523.255342 | 47000693 |
| 524.255044 | 4441217 |
| 524.258817 | 6431873 |
| 540.426364 | 15392057 |
| 541.429801 | 4342084 |
| 548.467852 | 9649554 |
| 551.355806 | 71347633 |
| 552.359301 | 17186236 |
| 554.551297 | 4041171 |
| 561.397903 | 7521818 |
| 567.279856 | 3884627 |
| 567.281570 | 48918099 |
| 567.283335 | 3735123 |
| 568.281346 | 4344413 |
| 568.285075 | 7269981 |
| 568.457668 | 5879390 |
| 582.403168 | 3354327 |
| 595.381995 | 51883826 |

| m/z | I |
|---|---|
| 596.385543 | 12308280 |
| 605.490292 | 5465959 |
| 611.307848 | 18460543 |
| 612.311269 | 3569539 |
| 619.439737 | 8830875 |
| 639.408421 | 26685376 |
| 640.411844 | 6768577 |
| 655.334193 | 8429510 |
| 677.481659 | 7190459 |
| 683.434624 | 10061750 |
| 685.435558 | 179482548 |
| 685.439070 | 6098868 |
| 686.439213 | 71135156 |
| 687.442918 | 9156531 |
| 699.360403 | 4435881 |
| 727.460746 | 4918177 |
| 735.523416 | 5835686 |
| 793.565191 | 3736147 |

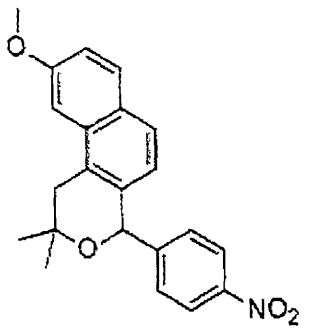


**38a-2**
Chemical Formula: $C_{22}H_{21}NO_4$
Molecular Weight: 363.41




| | | | | |
|---|---|---|---|---|
| PULSE SEQUENCE<br>Relax. delay 1.000 sec<br>Pulse 45.0 degrees<br>Acq. time 2.556 sec<br>Width 6410.3 Hz<br>4 repetitions | OBSERVE H1, 399.8399561 | DATA PROCESSING<br>FT size 32768<br>Total time 1 minute | | YC-142 pure pdt;<br>methoxy-diol with<br>4-nitro-benzaldehyde to<br>form tricyclic<br>isochromene; cdcl3;<br>6/10/2014<br>Solvent: cdcl3<br>Temperature |

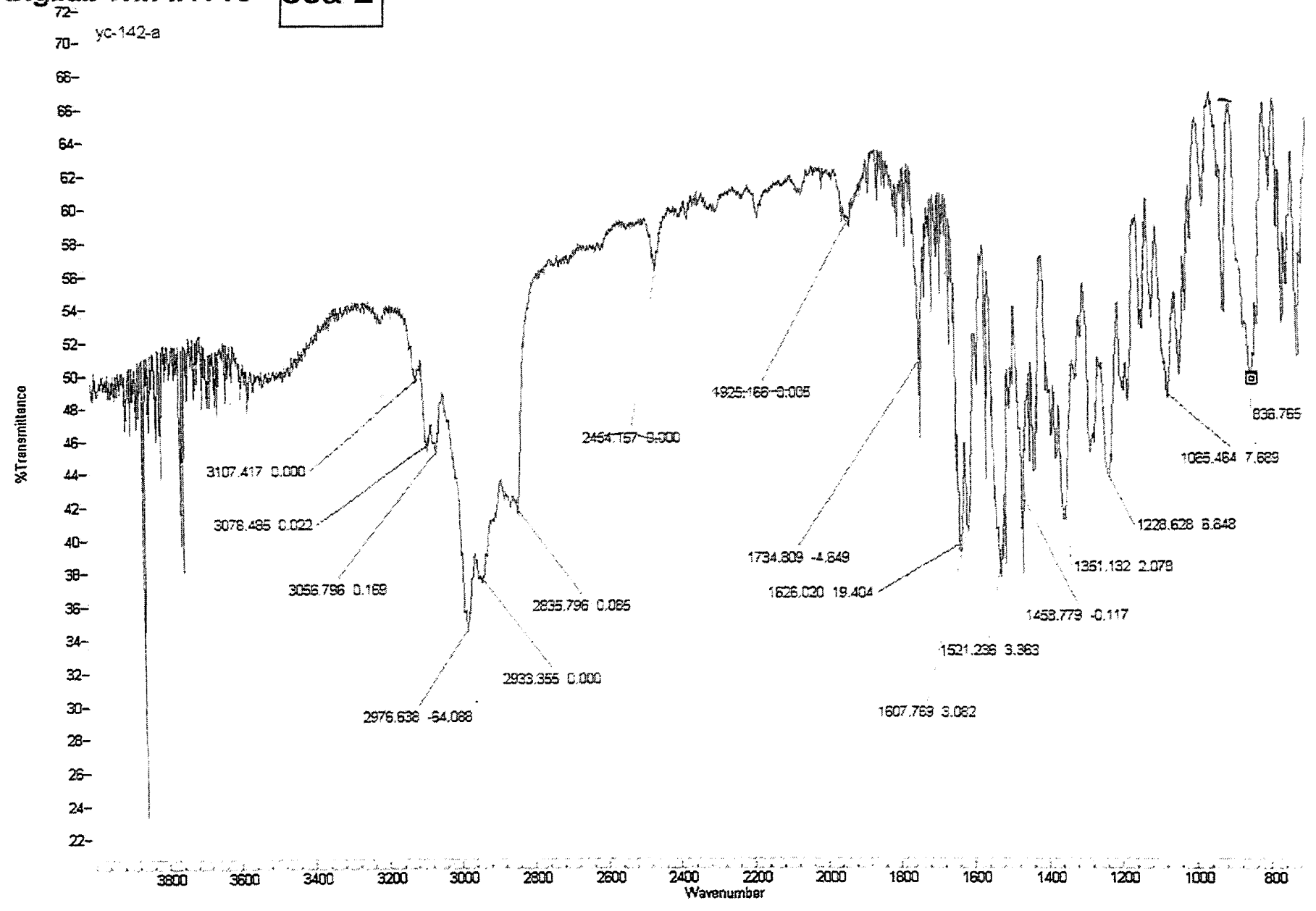
YC-142 pure pdt; methoxy-diol with 4-nitro-benzaldehyde to form tricyclic isochromene; cdcl3; 6/10/2014




**38a-2**

Chemical Formula: $C_{22}H_{21}NO_4$

Molecular Weight: 363.41


Digilab Win-IR Pro
38a-2
yc-142-a
%Transmittance
Wavenumber
3107.417 0.000
3078.485 0.022
3056.796 0.169
2976.638 -64.088
2933.355 0.000
2835.796 0.085
2454.757 -8.300
1925.166 -8.005
1734.809 -4.649
1626.020 19.404
1607.769 3.082
1521.296 3.363
1458.779 -0.117
1351.132 2.078
1228.628 6.648
1065.464 7.689
836.765

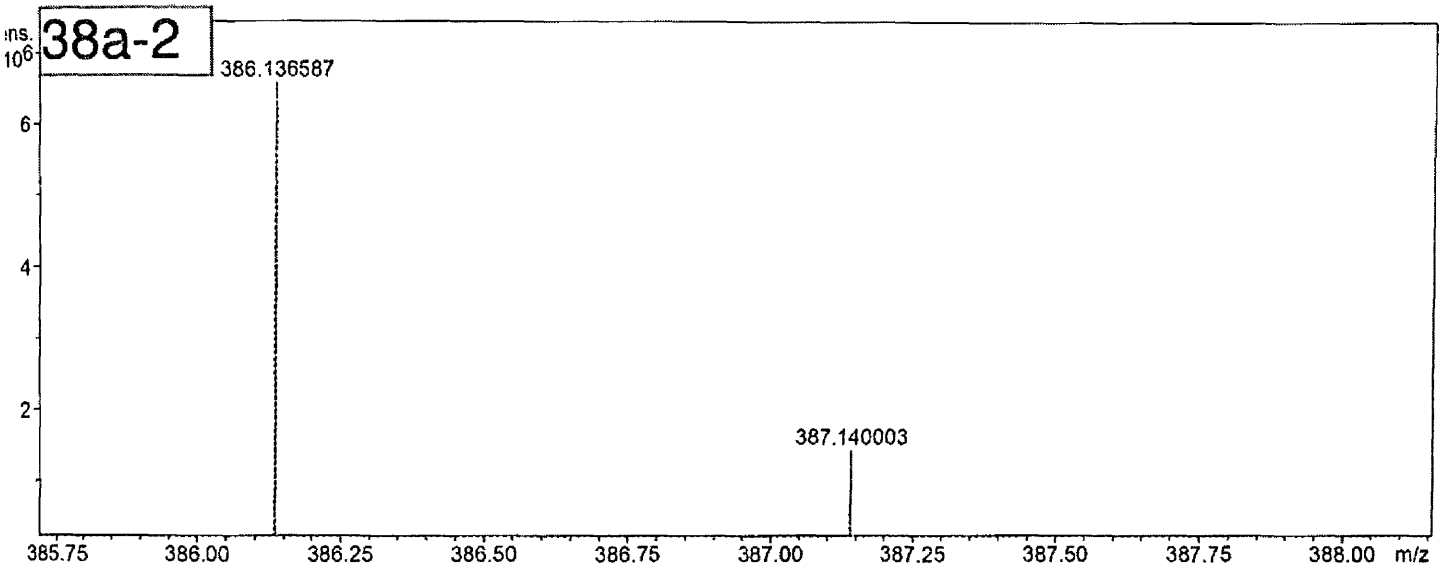
# Mass Spectrum List Report

**Analysis Info**

| | | | |
|---|---|---|---|
| Analysis Name | YC-142_pos_000001.d | Acquisition Date | 7/22/2014 3:34:49 PM |
| Method | XMASS_Method | Operator | FTMS_USER |
| Sample Name: | YC-142_pos | Instrument | apex-Qe |
| | YC-142_pos: in 1:1 THF:MeOH w/ NaCl.. | | |

**Acquisition Parameter**

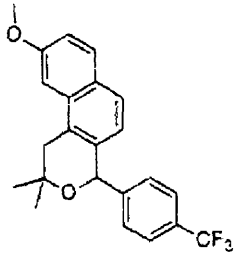
**Sample: YC-142**
**Exact Mass of = (C22H21NO4)Na+ : 386.136279u**
**Observed Mass = 386.136587u**
**Difference = < 1.0 ppm**




| m/z | I |
|---|---|
| 286.191675 | 3115859 |
| 288.288930 | 4718957 |
| 288.289853 | 61522797 |
| 289.292821 | 2802553 |
| 289.293244 | 20931449 |
| 304.284850 | 10361915 |
| 316.320056 | 7855324 |
| 316.321108 | 105227484 |
| 317.324048 | 4104426 |
| 317.324575 | 30065898 |
| 332.316151 | 23492020 |
| 333.319591 | 3288513 |
| 346.144075 | 8227432 |
| 360.324018 | 7168788 |
| 360.347520 | 2485012 |
| 364.154559 | 32511808 |
| 365.158012 | 5802827 |
| 372.347536 | 3210651 |
| 386.136587 | 6571052 |
| 413.264995 | 2479404 |
| 413.265538 | 5198124 |

| m/z | I |
|---|---|
| 413.266445 | 65530156 |
| 413.267357 | 5220652 |
| 414.269947 | 14047541 |
| 419.277156 | 12151137 |
| 420.280515 | 2507114 |
| 421.232902 | 26913138 |
| 422.236302 | 3727738 |
| 424.451723 | 3946893 |
| 425.287748 | 3597716 |
| 433.241197 | 2770903 |
| 435.202892 | 4023783 |
| 435.344876 | 6463976 |
| 437.192771 | 3451383 |
| 437.193729 | 35744247 |
| 438.197182 | 6494719 |
| 441.297897 | 14637592 |
| 442.301297 | 3064864 |
| 452.482920 | 4029041 |
| 463.303373 | 28355269 |
| 464.306830 | 5688013 |
| 479.121790 | 15010621 |
| 479.229002 | 33401662 |
| 480.125152 | 3412805 |
| 480.228702 | 3321670 |
| 480.232453 | 4542278 |
| 495.266211 | 34401207 |
| 496.269602 | 9071550 |
| 503.355925 | 3629043 |
| 507.224071 | 3363855 |
| 507.328297 | 3013648 |
| 507.329563 | 36801552 |
| 508.333022 | 8420376 |
| 523.255222 | 41643140 |
| 524.254952 | 3843211 |
| 524.258708 | 5914763 |
| 525.252220 | 2526866 |
| 540.426241 | 14150909 |
| 541.429699 | 3760388 |
| 548.467731 | 6716725 |
| 551.328931 | 4163912 |
| 551.355776 | 36719944 |
| 552.359202 | 8666447 |
| 553.390109 | 9213270 |
| 554.393454 | 2526045 |
| 554.551131 | 3214686 |
| 561.397764 | 9655692 |
| 567.281461 | 41266611 |
| 568.281210 | 3576249 |
| 568.284903 | 6997433 |
| 568.457513 | 4876730 |
| 569.278404 | 2618816 |
| 582.403074 | 2542100 |
| 595.381907 | 28667492 |
| 596.385380 | 6113898 |
| 611.307681 | 16023233 |
| 612.311066 | 2817222 |
| 619.439649 | 11665134 |
| 620.443050 | 2733812 |
| 639.408287 | 13913943 |
| 640.411601 | 3402588 |
| 655.333943 | 7610274 |

| m/z | I |
|---|---|
| 677.481501 | 9525246 |
| 683.434333 | 6430740 |
| 685.430142 | 2545692 |
| 685.431355 | 3964956 |
| 685.432723 | 6959132 |
| 685.435444 | 139505692 |
| 685.437888 | 11063324 |
| 685.439281 | 4841500 |
| 686.439049 | 57241631 |
| 686.441449 | 4239391 |
| 687.442683 | 7487523 |
| 699.360182 | 5075017 |
| 727.460245 | 2860176 |
| 735.523285 | 7717023 |
| 736.526128 | 2705057 |
| 793.564767 | 5991712 |
| 794.568010 | 2497315 |
| 851.606376 | 3177077 |

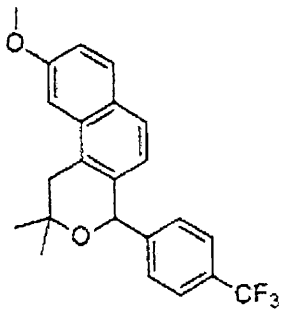


**38a-3**
Chemical Formula: $C_{23}H_{21}F_3O_2$
Molecular Weight: 386.41




| | | | | |
|---|---|---|---|---|
| PULSE SEQUENCE<br>Relax. delay 1.000 sec<br>Pulse 45.0 degrees<br>Acq. time 2.556 sec<br>Width 6410.3 Hz<br>4 repetitions | OBSERVE H1, 399.8398932 | DATA PROCESSING<br>FT size 32768<br>Total time 1 minute | | YC-144 pure pdt;<br>methoxy-diol with<br>4-CF3-benzaldehyde to<br>form tricyclic<br>isochromene; cdcl3;<br>6/10/2014<br>Solvent: cdcl3<br>Temperature |

YC-144 pure pdt; methoxy-diol with 4-CF3-benzaldehyde to form tricyclic isochromene; cdcl3; 6/10/2014

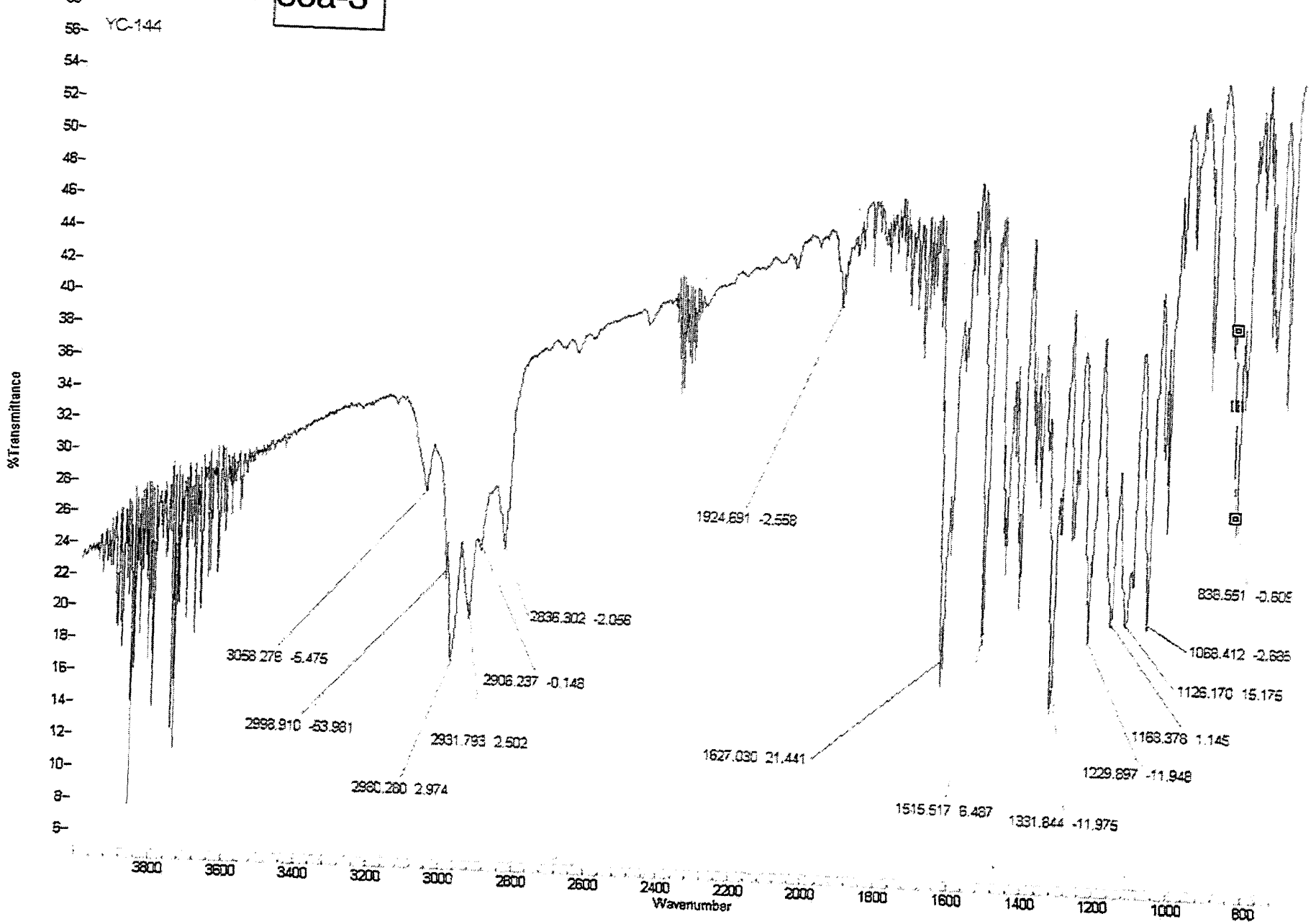


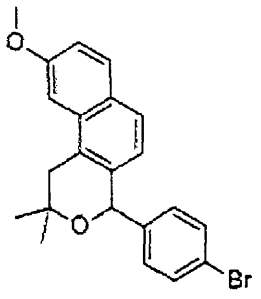
**38a-3**

Chemical Formula: $C_{23}H_{21}F_3O_2$

Molecular Weight: 386.41

Digilab Win-IR Pro 38a-3






**38a-4**

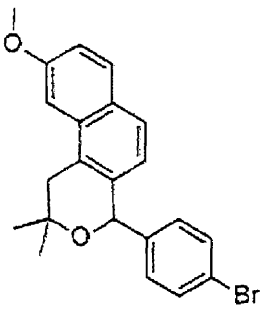
Chemical Formula: $C_{22}H_{21}BrO_2$

Molecular Weight: 397.31




| | | | | |
|---|---|---|---|---|
| PULSE SEQUENCE<br>Relax. delay 1.000 sec<br>Pulse 45.0 degrees<br>Acq. time 2.556 sec<br>Width 6410.3 Hz<br>8 repetitions | OBSERVE H1, 399.8398971 | DATA PROCESSING<br>FT size 32768<br>Total time 1 minute | | YC-79 pure pdt;<br>methoxy-diol with<br>4-Br-benzaldehyde to form<br>tricyclic isochromene;<br>cdcl3; 6/11/2014<br>127<br><br>Solvent: cdcl3<br>Ambient temperature |

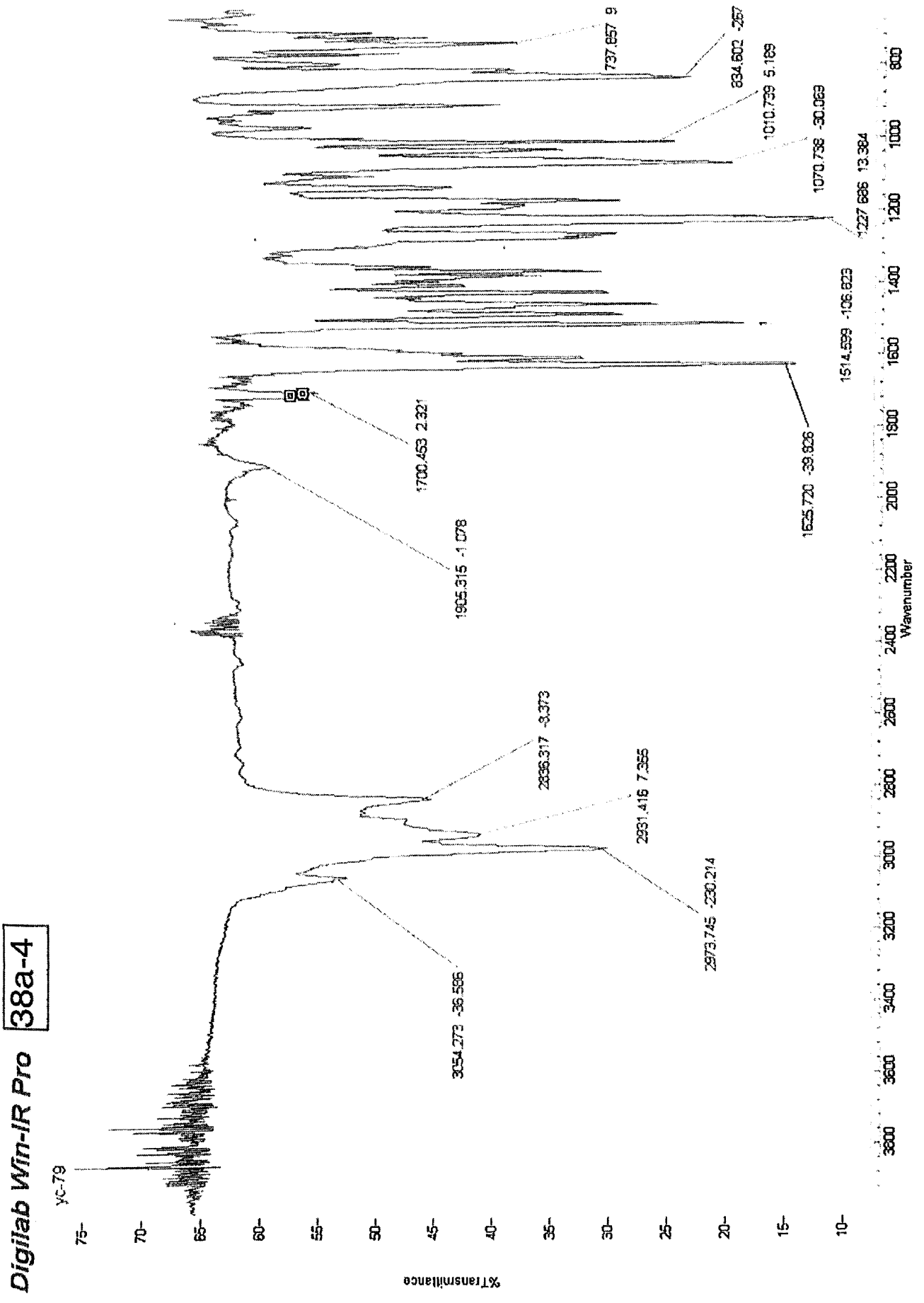
YC-79 pure pdt; methoxy-diol with 4-Br-benzaldehyde to form tricyclic isochromene; cdcl3; 6/11/2014




**38a-4**

Chemical Formula: $C_{22}H_{21}BrO_2$

Molecular Weight: 397.31


Digilab Win-IR Pro
38a-4
yc-79
%Transmittance
Wavenumber
3600
3400
3200
3000
2800
2600
2400
2200
2000
1800
1600
1400
1200
1000
800
3354.273 -36.586
2973.745 -230.214
2931.416 7.355
2836.317 -8.373
1905.315 -1.078
1700.453 2.321
1625.720 -39.926
1514.599 -106.823
1227.686 13.384
1070.738 -30.069
1010.739 5.169
834.602 -257
737.857 9

# Mass Spectrum List Report

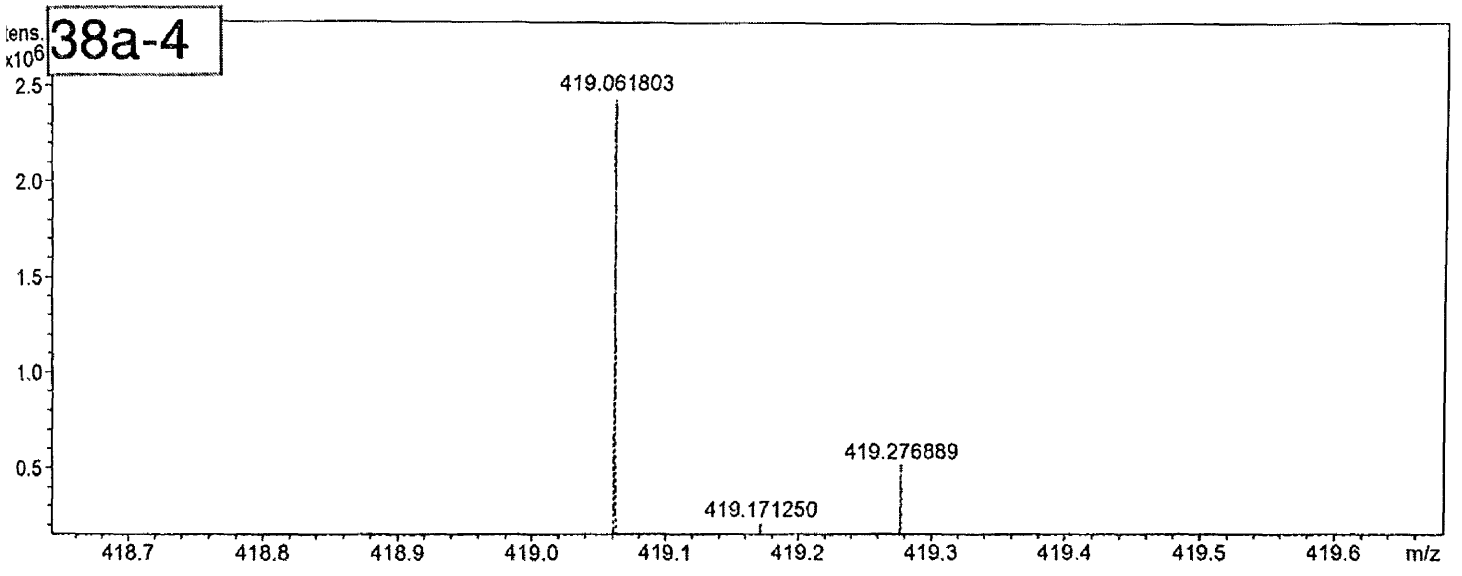


**Analysis Info**

| | | | |
|---|---|---|---|
| Analysis Name | YC-79_pos_000001.d | Acquisition Date | 7/22/2014 11:24:58 AM |
| Method | XMASS_Method | Operator | FTMS_USER |
| Sample Name: | YC-79_pos | Instrument | apex-Qe |
| | YC-79_pos: in 1:1 THF/MeOH w/ NaCl. | | |

**Acquisition Parameter**

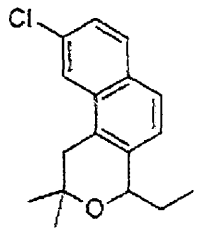
**Sample: YC-79**
**Exact Mass of = (C22H21BrO2)Na+ : 419.061714u**
**Observed Mass = 419.061803u**
**Difference = < 1.0 ppm**




| m/z | I |
|---|---|
| 209.440041 | 956572 |
| 215.089118 | 3091774 |
| 381.067247 | 867619 |
| 395.064210 | 1505140 |
| 397.062172 | 1247103 |
| 413.266335 | 3283671 |
| 419.061803 | 2448119 |
| 421.059762 | 2515713 |
| 430.389190 | 2424117 |
| 435.202567 | 1238096 |
| 435.344570 | 1213009 |
| 437.193502 | 6100827 |
| 438.196911 | 1596769 |
| 441.297566 | 2613107 |
| 452.482664 | 913847 |
| 453.167455 | 2738620 |
| 463.197464 | 977917 |
| 463.303052 | 2868222 |
| 469.328874 | 3910696 |
| 470.332242 | 1113904 |
| 477.267083 | 1306212 |

| m/z | I |
|---|---|
| 479.228755 | 4871283 |
| 480.232167 | 916091 |
| 485.302801 | 861091 |
| 497.360142 | 804104 |
| 507.223603 | 863582 |
| 507.329234 | 5057887 |
| 508.332620 | 1403240 |
| 517.371166 | 940985 |
| 521.293252 | 1564124 |
| 523.254878 | 9239022 |
| 524.254528 | 1388791 |
| 524.258291 | 1826807 |
| 525.251827 | 798464 |
| 540.425867 | 1108871 |
| 549.246859 | 906196 |
| 550.628475 | 2932447 |
| 551.355360 | 7920358 |
| 551.631847 | 1087976 |
| 552.358679 | 2296558 |
| 554.371227 | 925183 |
| 561.397317 | 1343033 |
| 563.262453 | 978248 |
| 565.319425 | 1193048 |
| 567.281010 | 12430183 |
| 568.280705 | 1792367 |
| 568.284461 | 2526063 |
| 569.277924 | 1099383 |
| 583.392238 | 910812 |
| 595.381464 | 8166438 |
| 596.384923 | 2327084 |
| 605.365886 | 1973338 |
| 605.423464 | 1284443 |
| 609.345578 | 820589 |
| 611.307161 | 12369013 |
| 612.306871 | 1288058 |
| 612.310594 | 3050618 |
| 612.413130 | 1620090 |
| 612.914610 | 889980 |
| 613.304049 | 1049982 |
| 633.397178 | 1024707 |
| 639.407729 | 5692627 |
| 640.411090 | 1986261 |
| 641.433881 | 1949400 |
| 641.935643 | 1424601 |
| 649.449526 | 1269993 |
| 655.333346 | 9088243 |
| 656.332902 | 1090804 |
| 656.336734 | 2279156 |
| 657.330175 | 850422 |
| 661.428382 | 1140988 |
| 663.453506 | 2986238 |
| 664.456812 | 1303807 |
| 670.454855 | 1953542 |
| 670.956417 | 1311494 |
| 677.480802 | 824075 |
| 683.433784 | 2978063 |
| 684.437147 | 1073168 |
| 685.432635 | 963856 |
| 685.435254 | 12635408 |
| 685.437871 | 852240 |
| 686.438741 | 4791569 |

| m/z | I |
|---|---|
| 687.442101 | 1052689 |
| 699.359487 | 5371157 |
| 699.475699 | 1561365 |
| 699.977397 | 1130773 |
| 700.362886 | 1295637 |
| 701.409262 | 2032917 |
| 702.412652 | 795669 |
| 727.459926 | 1142038 |
| 728.496527 | 1608982 |
| 728.998328 | 1173271 |
| 743.385563 | 2405656 |
| 757.517521 | 1242911 |
| 758.019104 | 992031 |
| 787.411869 | 834886 |
| 861.539934 | 979145 |
| 877.534690 | 6260568 |
| 878.537984 | 3355489 |
| 879.541454 | 845675 |




**38b-1**

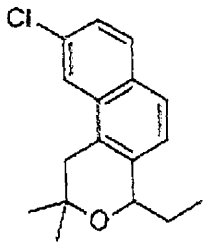
Chemical Formula: $C_{17}H_{13}ClO$

Molecular Weight: 274.79




| | | | | |
|---|---|---|---|---|
| PULSE SEQUENCE<br>Relax. delay 1.000 sec<br>Pulse 45.0 degrees<br>Acq. time 2.556 sec<br>Width 6410.3 Hz<br>8 repetitions | OBSERVE H1, 399.8398892 | DATA PROCESSING<br>FT size 32768<br>Total time 1 minute | | YC-138 pure pdt; cl-sub. alkynediol with propionaldehyde to form tricyclic isochromene; cdcl3; 7/19/2014 133<br>Solvent: cdcl3<br>Temp. 20.0 C / 293.1 K |

YC-138 pure pdt; cl-diol with propionaldehyde to form tricyclic isochromene; cdcl3; 6/8/2014

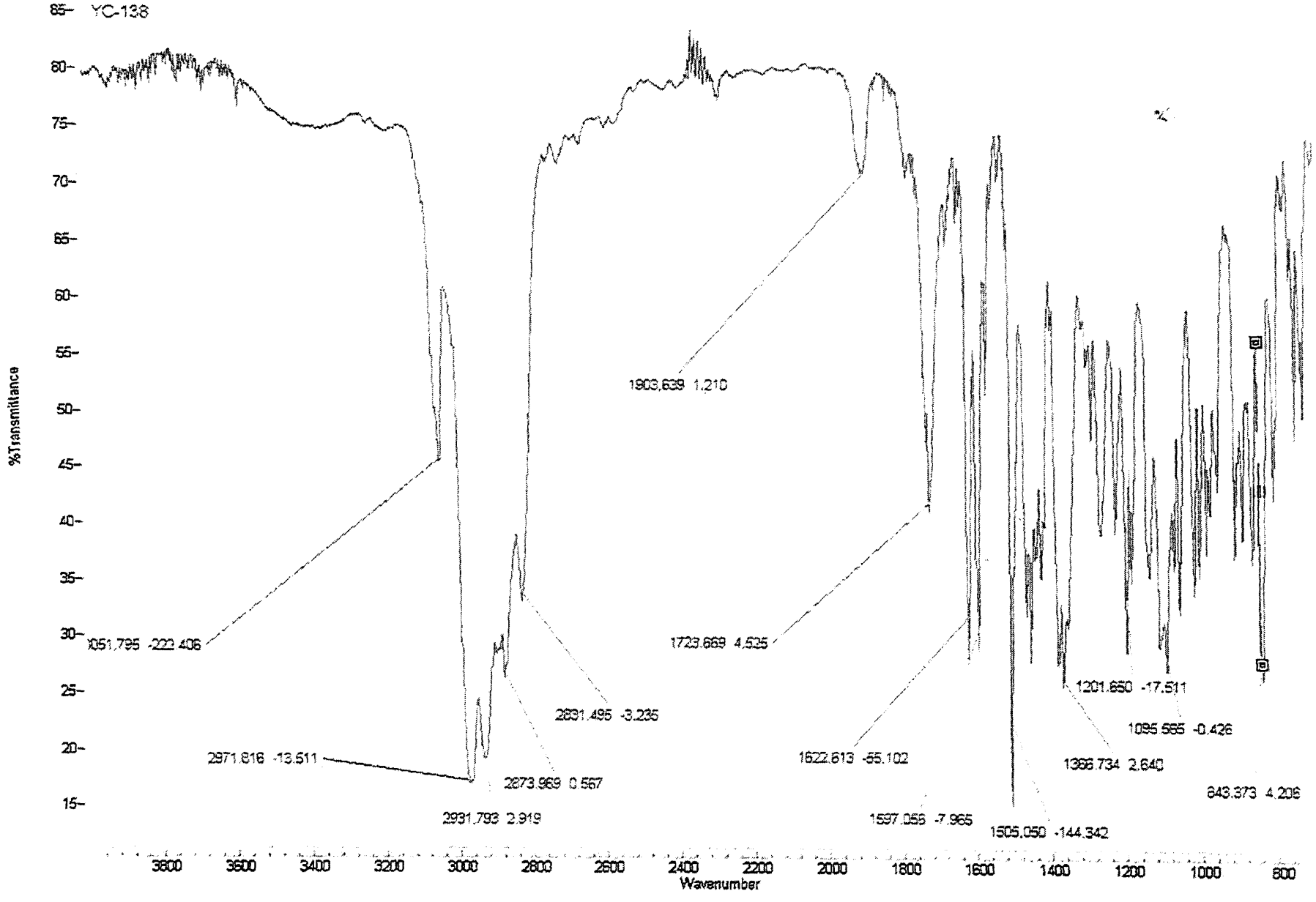


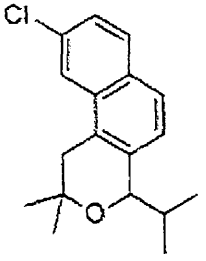

**38b-1**

Chemical Formula: $C_{17}H_{13}ClO$

Molecular Weight: 274.79

*Digilab Win-IR Pro* **38b-1**






**38b-2**

Chemical Formula: $C_{18}H_{21}ClO$

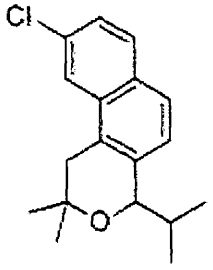
Molecular Weight: 288.82




| | | | | |
|---|---|---|---|---|
| PULSE SEQUENCE<br>Relax. delay 1.000 sec<br>Pulse 45.0 degrees<br>Acq. time 2.556 sec<br>Width 6410.3 Hz<br>8 repetitions | OBSERVE H1, 399.8398932 | DATA PROCESSING<br>FT size 32768<br>Total time 1 minute | | YC-139 pure pdt; cl-diol with isobutyraldehyde to form tricyclic isochromene; cdcl3; 6/8/2014<br>Solvent: cdcl3<br>Ambient temperature |

YC-139 pure pdt; cl-diol with isobutyraldehyde to form tricyclic isochromene; cdcl3; 6/8/2014

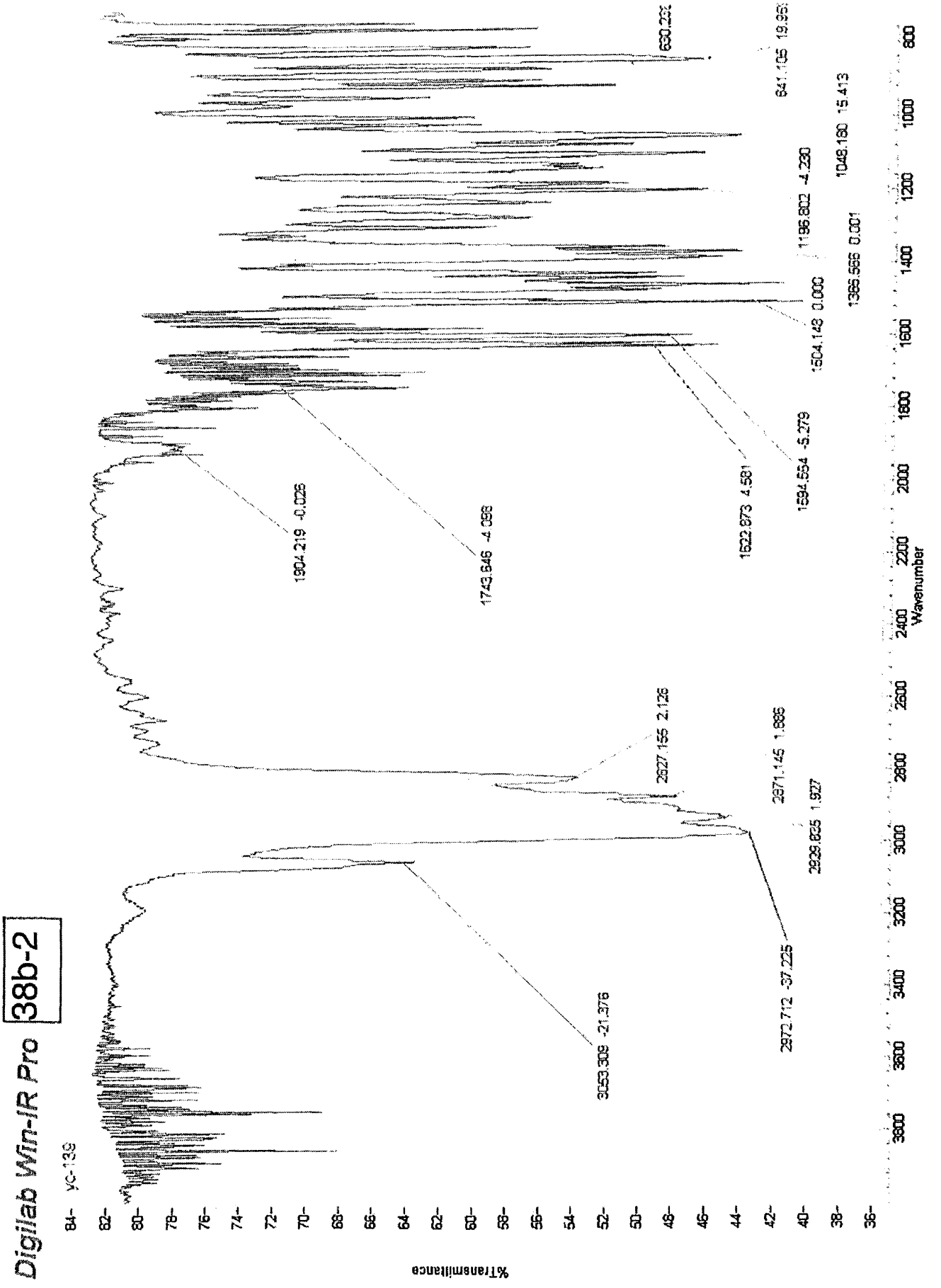
Sample Name:
YC-139-pdt

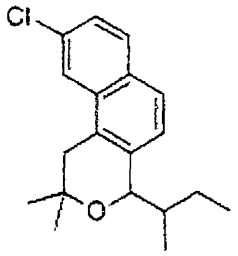



**38b-2**

Chemical Formula: $C_{18}H_{21}ClO$

Molecular Weight: 288.82


Digilab Win-IR Pro
38b-2
yc-138
%Transmittance
Wavenumber
3800
3600
3400
3200
3000
2800
2600
2400
2200
2000
1800
1600
1400
1200
1000
800
84
82
80
78
76
74
72
70
68
66
64
62
60
58
56
54
52
50
48
46
44
42
40
38
36
3353.309 -21.376
2972.712 -37.225
2928.635 1.927
2871.145 1.886
2627.155 2.126
1904.219 -0.026
1743.646 -4.098
1622.873 4.581
1594.554 -5.279
1504.148 0.000
1396.566 0.001
1196.802 -4.230
1048.180 15.413
841.105 19.95
650.22



**38b-3**

Chemical Formula: $C_{19}H_{23}ClO$

Molecular Weight: 302.84



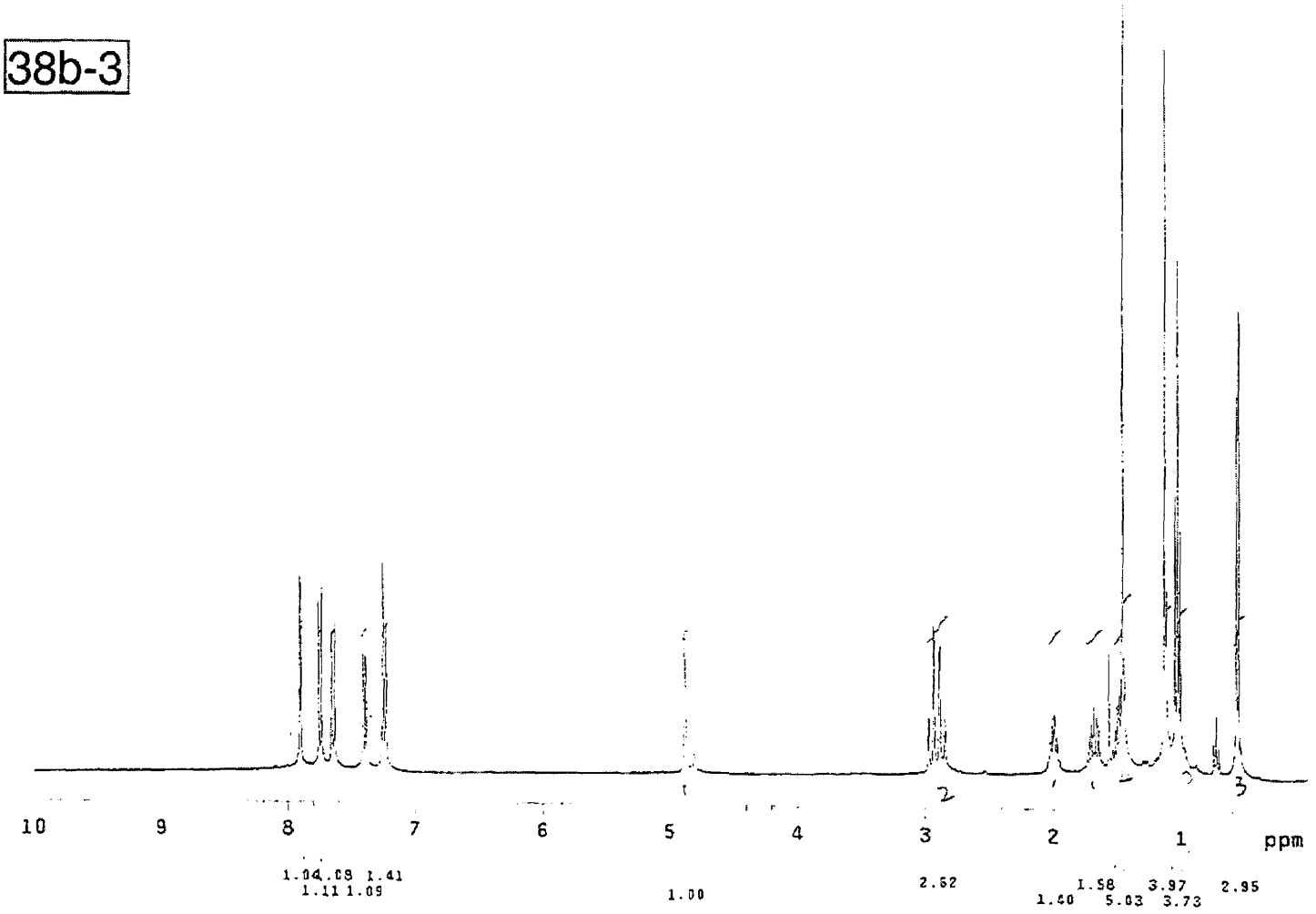

| | | | | |
|---|---|---|---|---|
| PULSE SEQUENCE<br>Relax. delay 1.000 sec<br>Pulse 14.8 degrees<br>Acq. time 1.998 sec<br>Width 6402.0 Hz<br>16 repetitions | OBSERVE H1, 400.1766844 | DATA PROCESSING<br>FT size 32768<br>Total time 1 minute | | YC-122 mixture; cl-diol with 2-methylbutyraldehyde to form tricyclic isochromene; cdcl3; 3/13/2014<br>Solvent : CDCl3<br>Ambient temperature |

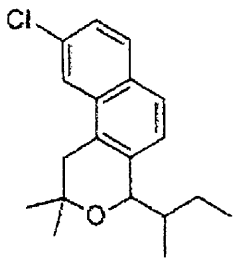
YC-122 purified the 3th time; fr2 ; ci-diol with 2-methyl-butyraldehyde to form tricyclic isochromene; cdcl3; 3/12/2014

Automation directory:

Pulse Sequence: s2pul

38b-3

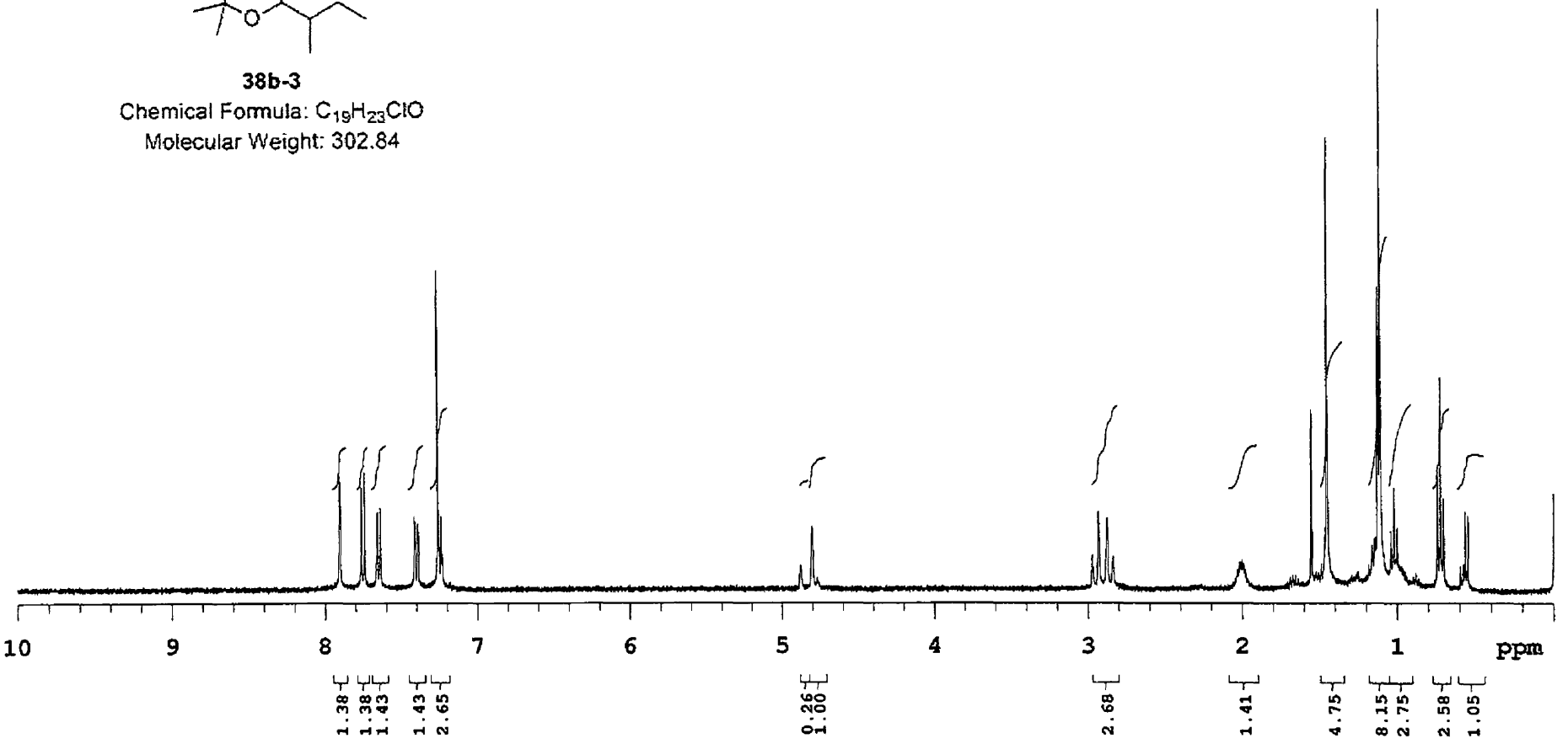





**38b-3**

Chemical Formula: $C_{19}H_{23}ClO$

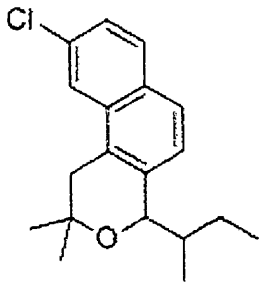
Molecular Weight: 302.84




| | | | | |
|---|---|---|---|---|
| PULSE SEQUENCE<br>Relax. delay 1.000 sec<br>Pulse 14.8 degrees<br>Acq. time 1.998 sec<br>Width 6402.0 Hz<br>16 repetitions | OBSERVE H1, 400.1766813 | DATA PROCESSING<br>FT size 32768<br>Total time 1 minute | | YC-122 purified the 3th time; fr3 ; cl-diol with 2-methyl-butyraldehyde to form tricyclic isochromene; cdcl3; 3/12/2014<br>Solvent: CDCl3<br>Temperature |

YC-122 mixture; cl-diol with 2-methylbutyraldehyde to form tricyclic isochromene; cdcl3; 3/13/2014

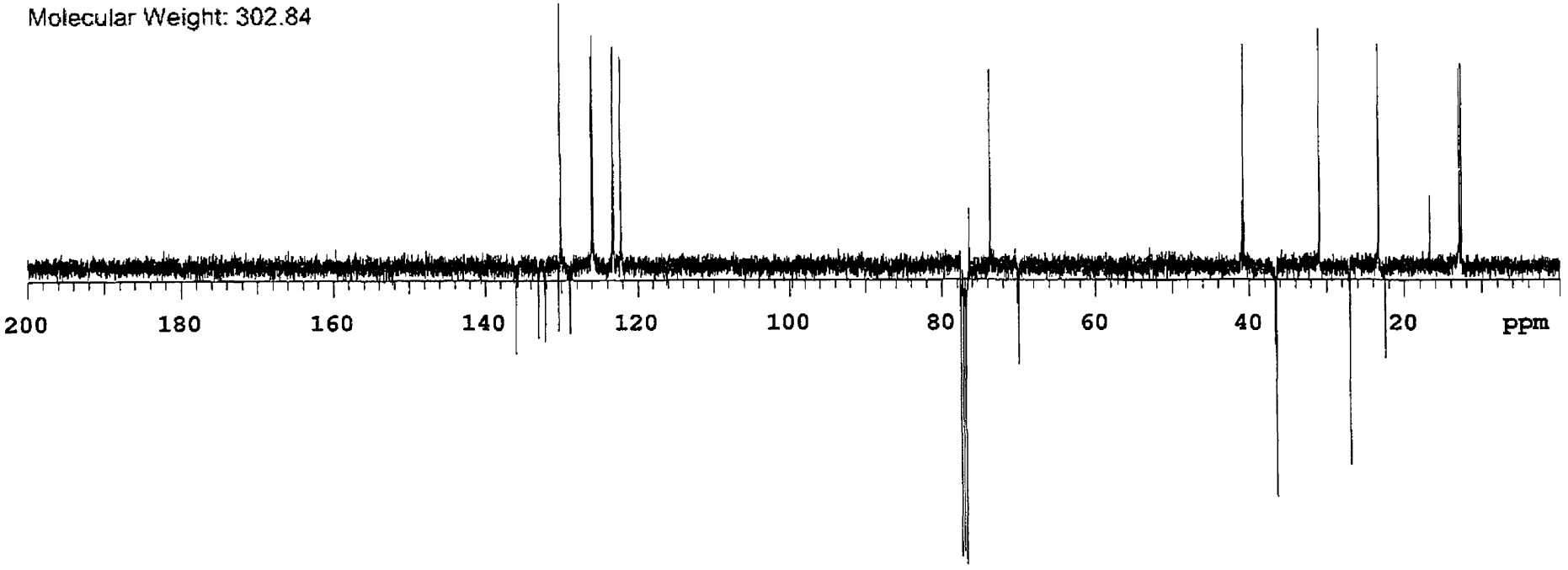
Sample Name:
yc-122-mixture




**38b-3**

Chemical Formula: $C_{19}H_{23}ClO$

Molecular Weight: 302.84

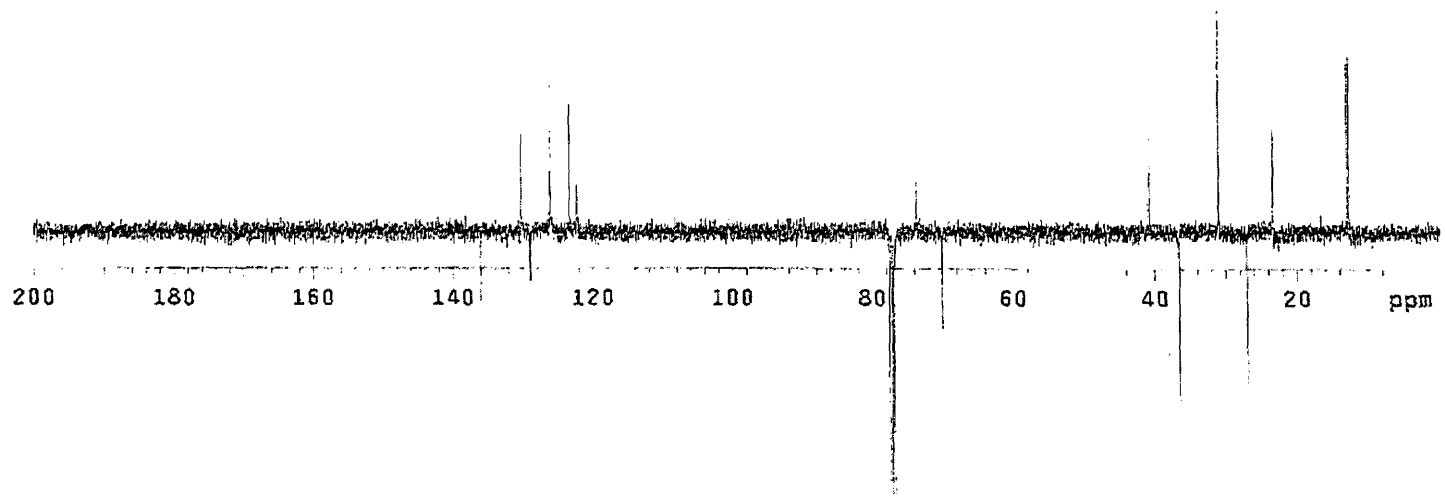


YC-122 pure; cl-diol with 2-methyl-butyraldehyde to form tricyclic isochromene; cdcl3; 3/12/2014

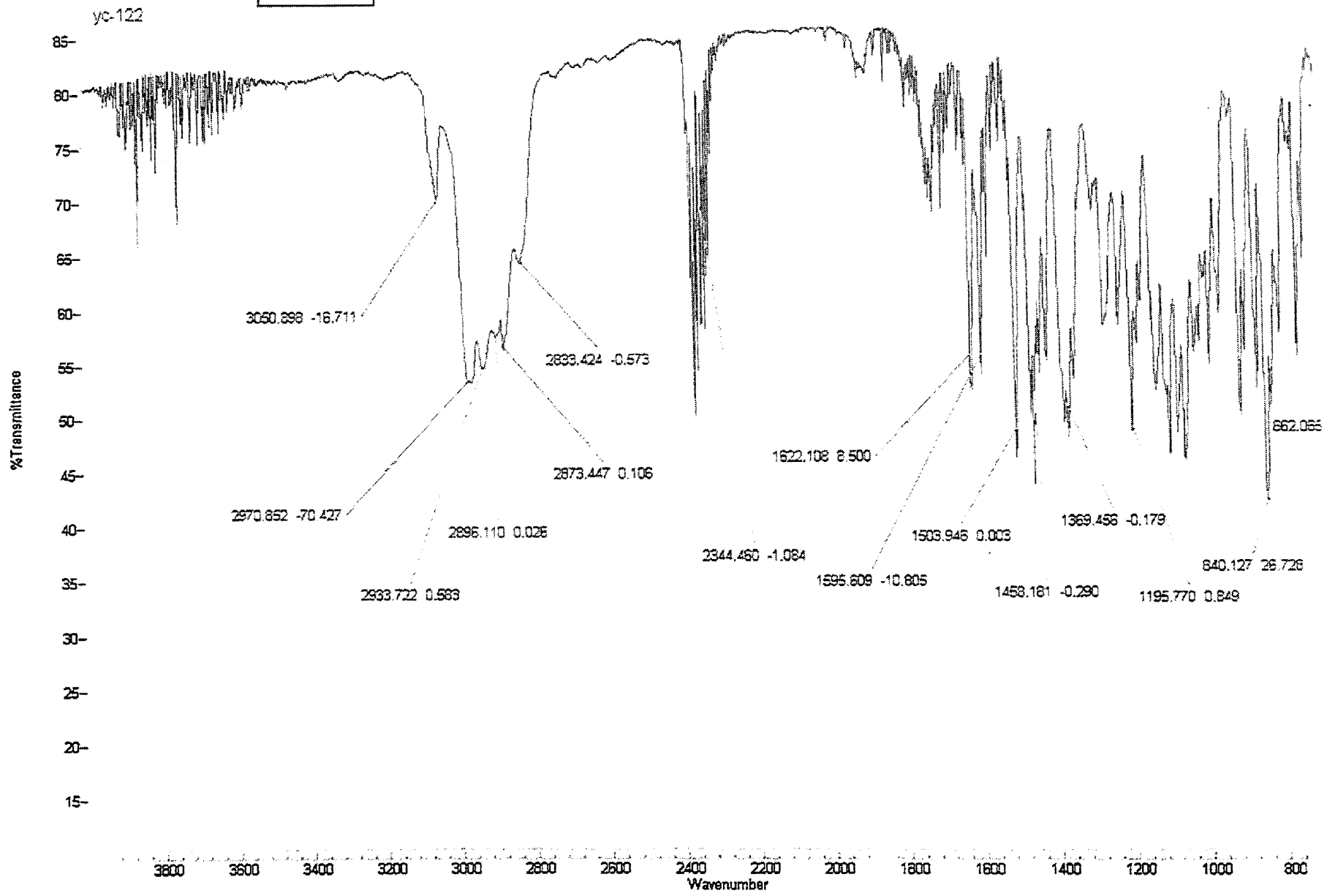
Automation directory:

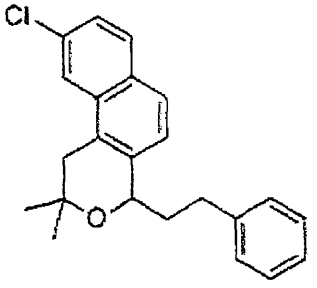
Pulse Sequence: APT

38b-3



Digilab Win-IR Pro 38b-3






**38b-4**

Chemical Formula: $C_{23}H_{23}ClO$

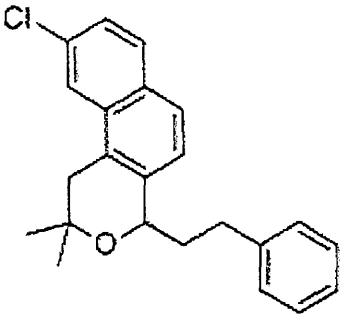
Molecular Weight: 350.89




| | | | | |
|---|---|---|---|---|
| PULSE SEQUENCE<br>Relax. delay 1.000 sec<br>Pulse 45.0 degrees<br>Acq. time 2.556 sec<br>Width 6410.3 Hz<br>8 repetitions | OBSERVE H1, 399.8399581 | DATA PROCESSING<br>FT size 32768<br>Total time 1 minute | | YC-141 pure pdt; cl-diol with phenylpropionaldehyde to form tricyclic isochromene; cdcl3; 6/8/2014<br>Solvent: cdcl3<br>Ambient temperature |

YC-141 pure pdt; cl-diol with phenylpropionaldehyde to form tricyclic isochromene; cdcl3; 6/8/2014

Sample Name:
YC-141-pdt

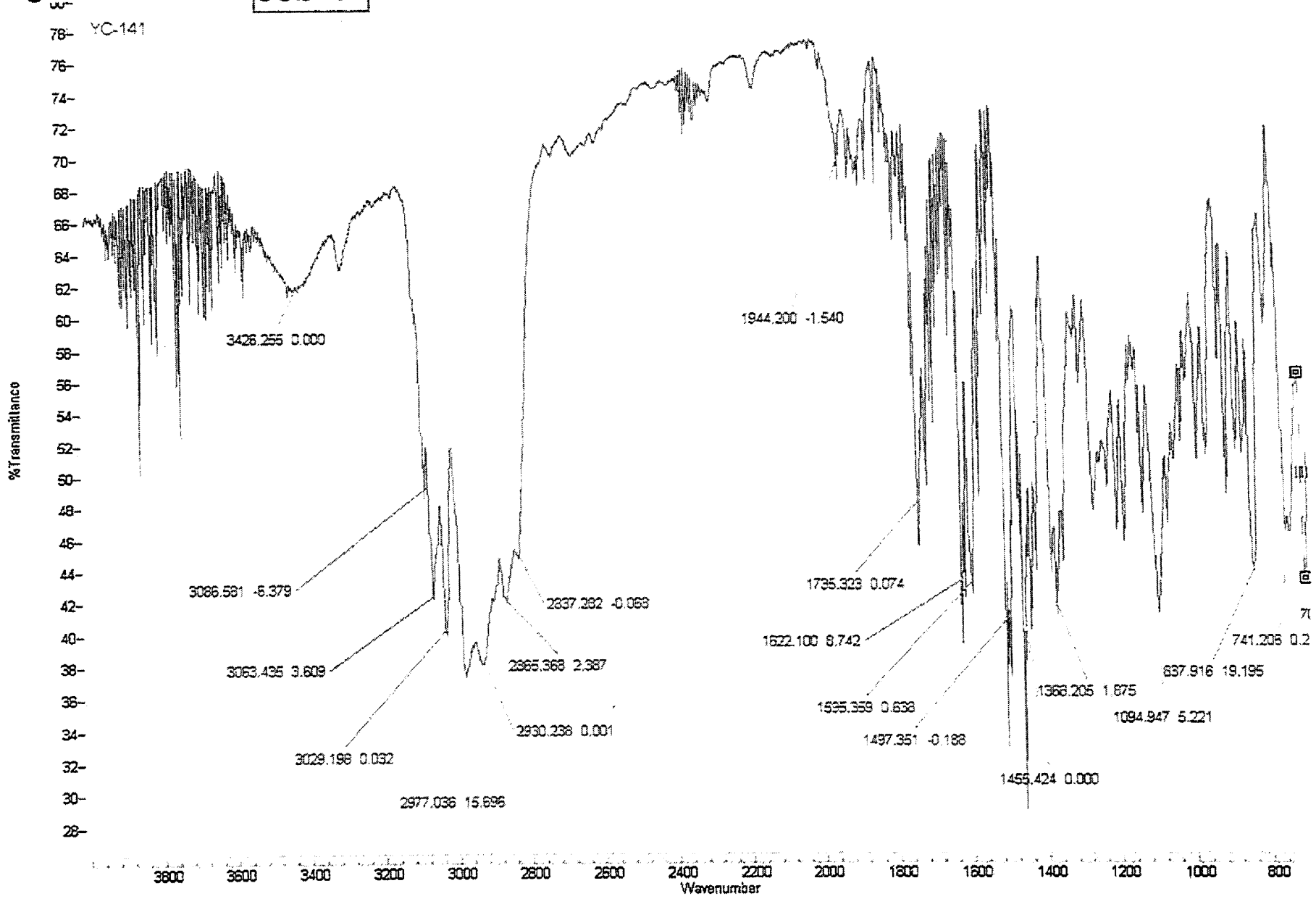


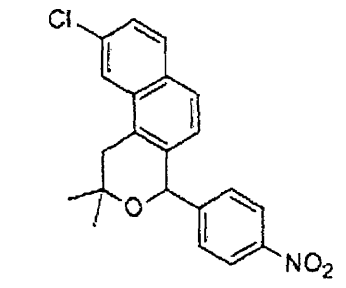

**38b-4**

Chemical Formula: $C_{23}H_{23}ClO$

Molecular Weight: 350.89

Digilab Win-IR Pro 38b-4






**38b-5**

Chemical Formula: $C_{21}H_{18}ClNO_3$

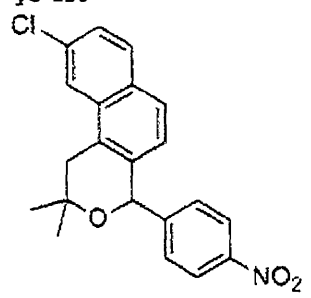
Molecular Weight: 367.83




| | | | | |
|---|---|---|---|---|
| PULSE SEQUENCE<br>Relax. delay 1.000 sec<br>Pulse 45.0 degrees<br>Acq. time 2.556 sec<br>Width 6410.3 Hz<br>16 repetitions | OBSERVE H1, 399.8398896 | DATA PROCESSING<br>FT size 32768<br>Total time 1 minute | | YC-136 pure pdt; cl-sub. alkynediol with p-nitro-benzaldehyde to form tricyclic isochromenes; cdcl3; 7/19/2014<br>148<br>Solvent: cdcl3 293.1 K |

YC-136 pure pdt; cl-diol with p-nitro-benzaldehyde to form tricyclic isochromene; cdcl3; 6/17/2014

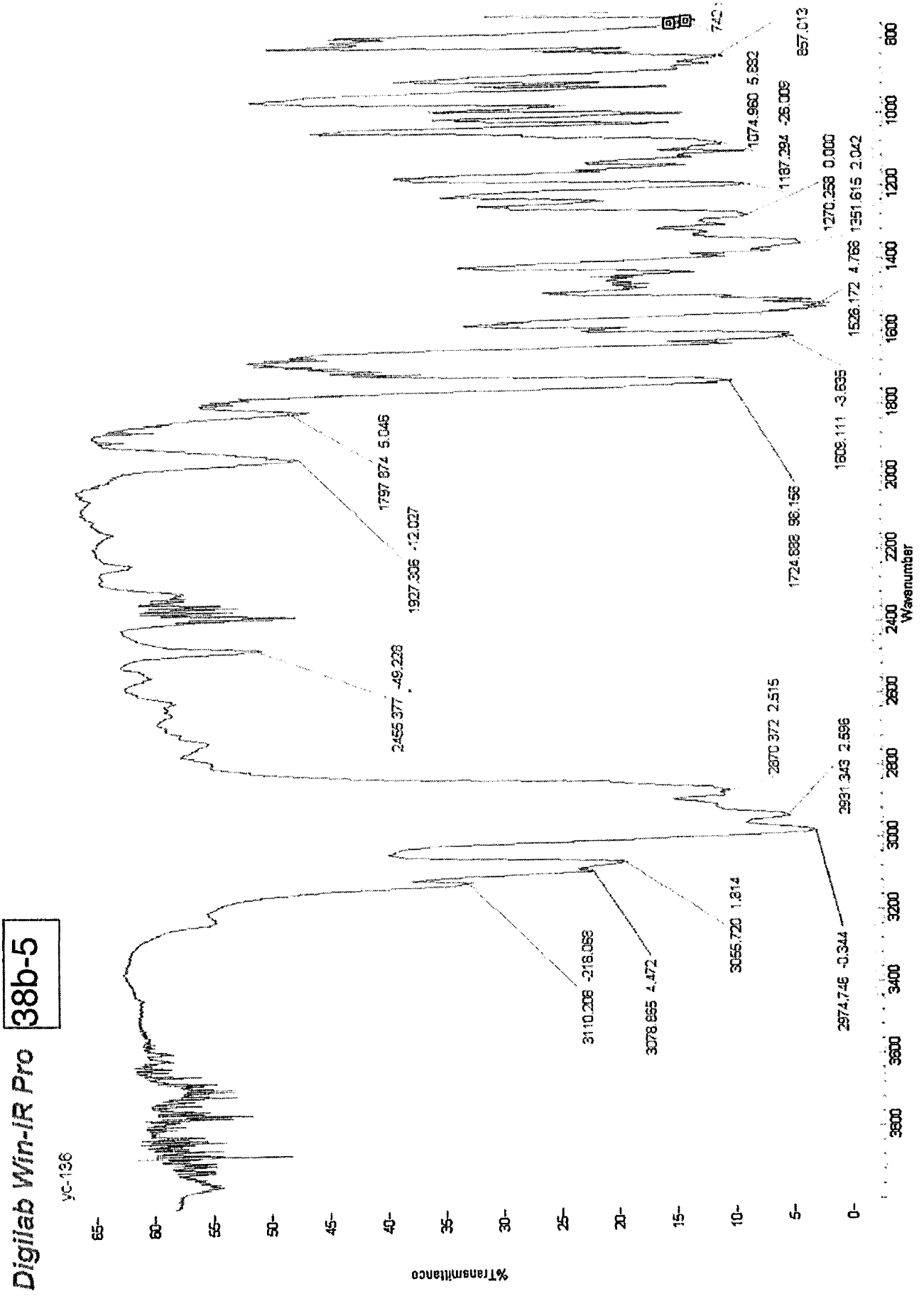
Sample Name:
yc-136

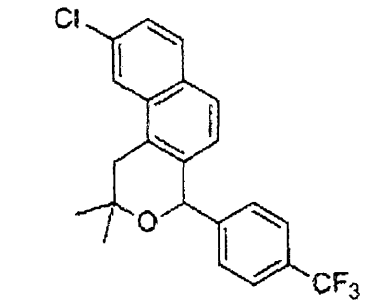



**38b-5**

Chemical Formula: $C_{21}H_{18}ClNO_3$

Molecular Weight: 367.83


Digilab Win-IR Pro
38b-5
yc-136
%Transmittance
Wavenumber
3600
3400
3200
3000
2800
2600
2400
2200
2000
1800
1600
1400
1200
1000
800
65
60
55
50
45
40
35
30
25
20
15
10
5
0
3110.206 -218.068
3078.865 4.472
3055.720 1.814
2974.745 -0.344
2931.343 2.596
2870.372 2.515
2455.377 -49.228
1927.305 -12.027
1797.874 5.046
1724.888 96.156
1609.111 -3.635
1526.172 4.766
1351.615 2.042
1270.258 0.000
1187.294 -26.009
1074.960 5.832
857.013




**38b-6**

Chemical Formula: $C_{22}H_{18}ClF_3O$

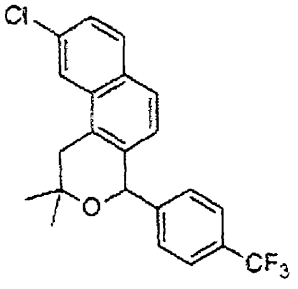
Molecular Weight: 390.83




| | | | | |
|---|---|---|---|---|
| PULSE SEQUENCE<br>Relax. delay 1.000 sec<br>Pulse 45.0 degrees<br>Acq. time 2.556 sec<br>Width 6410.3 Hz<br>8 repetitions | OBSERVE H1, 399.8399018 | DATA PROCESSING<br>FT size 32768<br>Total time 1 minute | | YC-137 pure pdt; cl-diol with 4-CF3-benzaldehyde to form tricyclic isochromene; cdcl3; 6/8/2014<br>Solvent: cdcl3<br>Ambient temperature |

YC-137 pure pdt; cl-diol with 4-CF3-benzaldehyde to form tricyclic isochromene; cdcl3; 6/8/2014

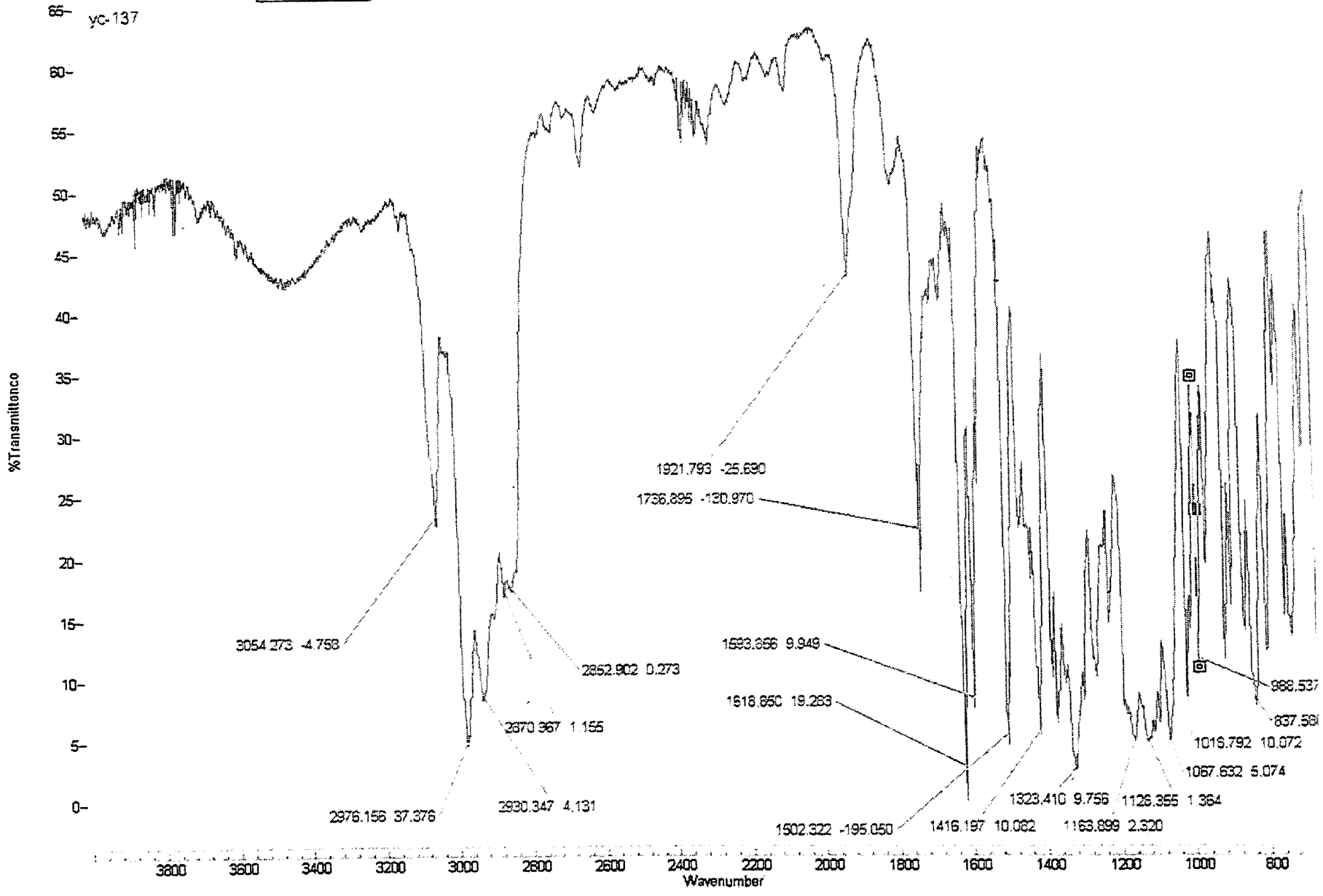
Sample Name:
YC-137-pdt

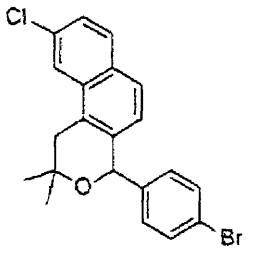



**38b-6**

Chemical Formula: $C_{22}H_{18}ClF_3O$
Molecular Weight: 390.83

*Digilab Win-IR Pro* 38b-6

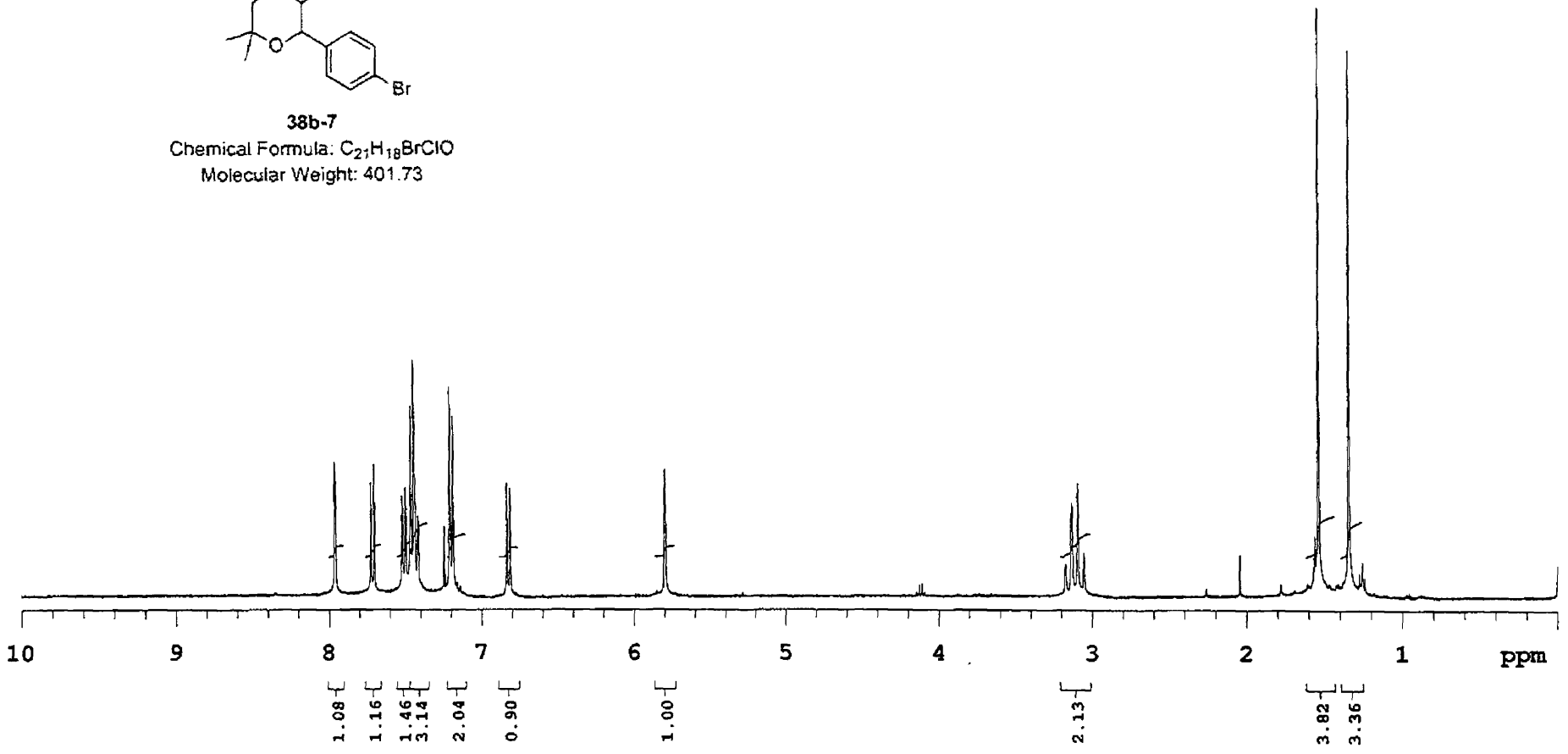





**38b-7**

Chemical Formula: $C_{21}H_{18}BrClO$

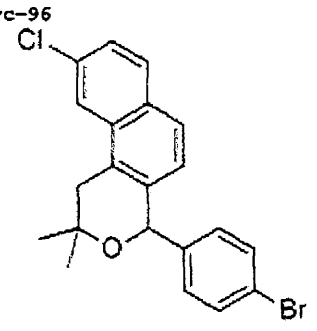
Molecular Weight: 401.73




| | | | | |
|---|---|---|---|---|
| PULSE SEQUENCE<br>Relax. delay 1.000 sec<br>Pulse 14.8 degrees<br>Acq. time 1.998 sec<br>Width 6402.0 Hz<br>16 repetitions | OBSERVE H1, 400.1766864 | DATA PROCESSING<br>FT size 32768<br>Total time 1 minute | | YC-96 pure<br>4-(4-bromophenyl)-9-chloro<br>-2,2-dimethyl-1,4-dihydro-<br>2-H-benzo[f]isochromene;<br>CDCl3; 9/12/20<br>Solvent: CDCl3<br>Ambient temperature |

YC-96 pure 4-(4-bromophenyl)-9-chloro-2,2-dimethyl-1,4-dihydro-2-H-benzo[f]isochromene; CDCl3; 9/12/2013

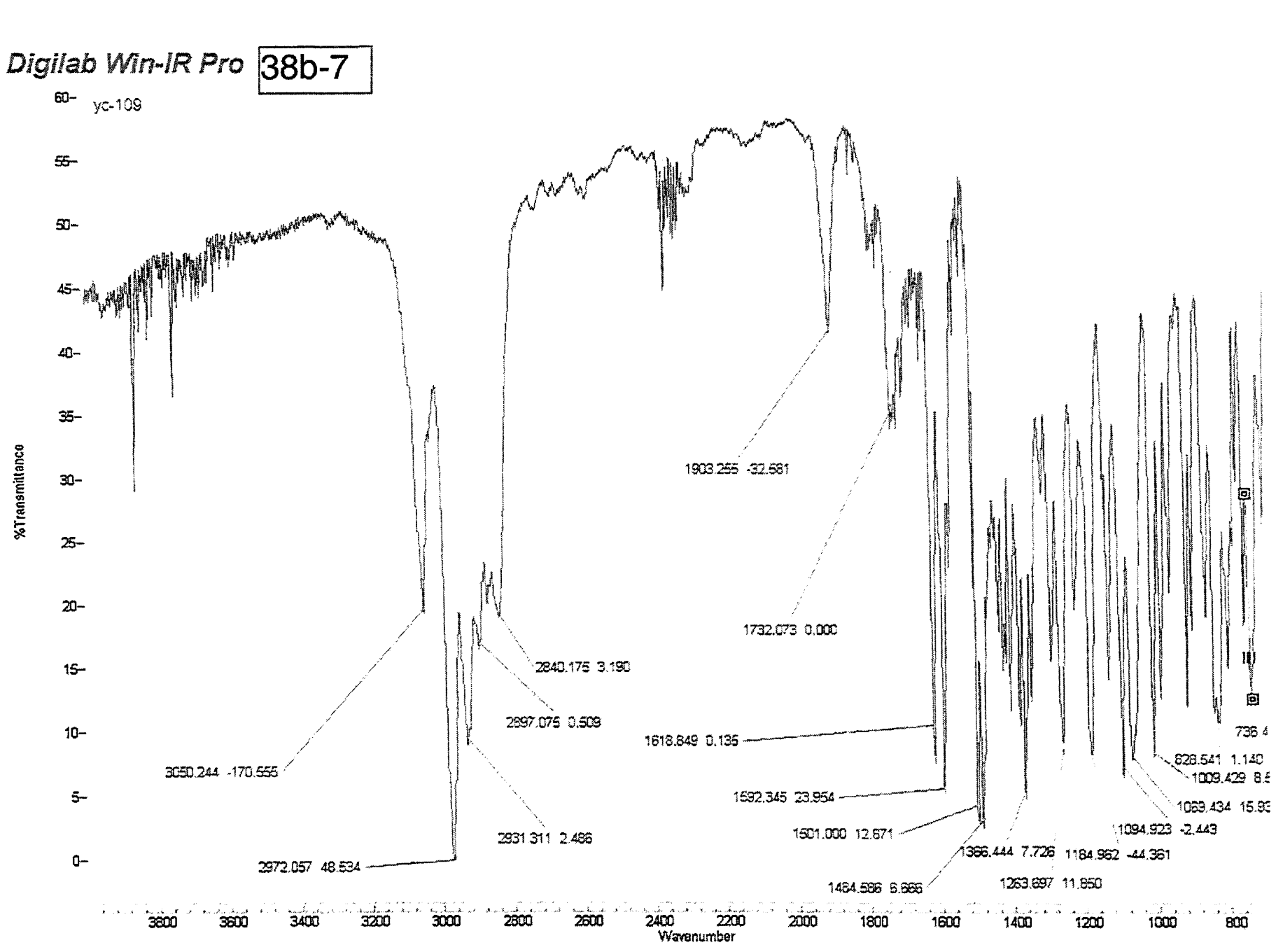
Sample Name:
yc-96




**38b-7**

Chemical Formula: $C_{21}H_{18}BrClO$

Molecular Weight: 401.73


Digilab Win-IR Pro
38b-7
yc-109
%Transmittance
Wavenumber
3050.244 -170.555
2972.057 48.534
2931.311 2.486
2897.075 0.509
2840.175 3.190
1903.255 -32.581
1732.073 0.000
1618.849 0.135
1592.345 23.954
1601.000 12.671
1484.586 6.666
1366.444 7.726
1263.697 11.850
1184.962 -44.361
1094.923 -2.443
1069.434 15.93
1009.429 8.5
828.541 1.140
736.4

# Mass Spectrum List Report

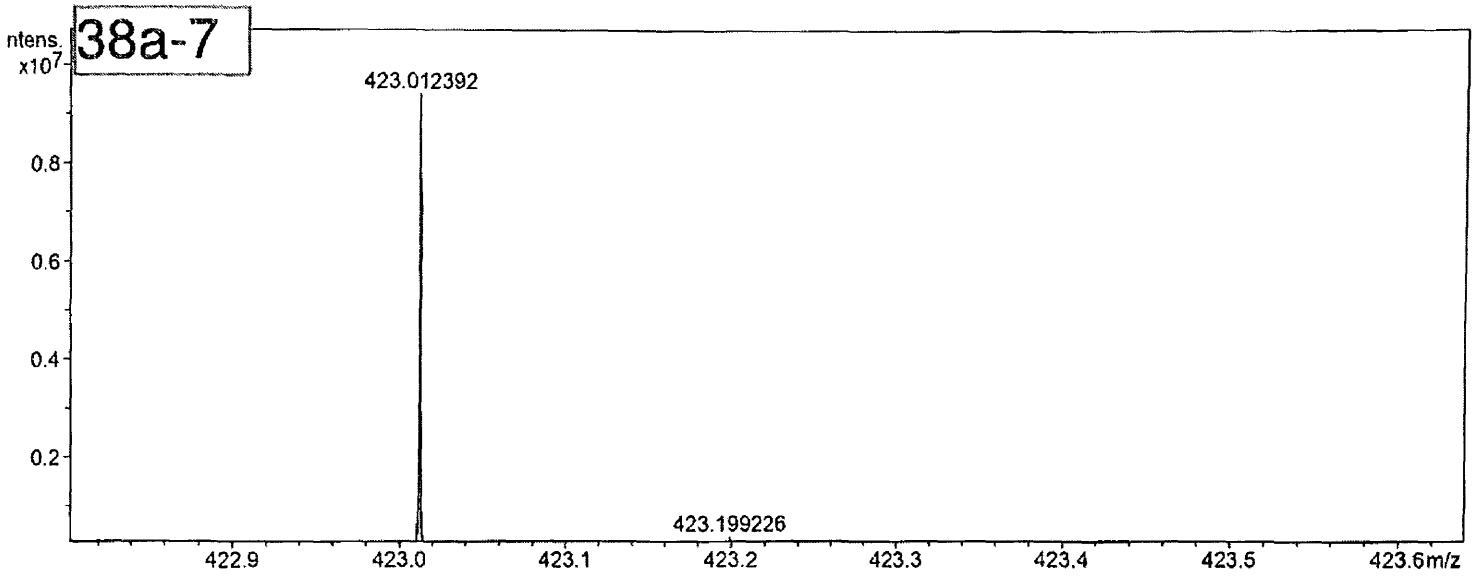


**Analysis Info**

| | | | |
|---|---|---|---|
| Analysis Name | YC-135_pos_000001.d | Acquisition Date | 7/22/2014 11:39:22 AM |
| Method | XMASS_Method | Operator | FTMS_USER |
| Sample Name: | YC-135_pos | Instrument | apex-Qe |
| | YC-135_pos: in 1:1 THF/MeOH w/ NaCl. | | |

**Acquisition Parameter**

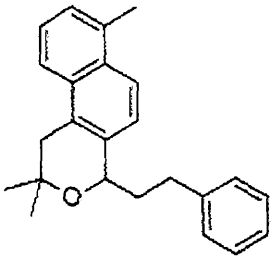
**Sample: YC-135**
**Exact Mass of = (C21H18BrClO)Na+ : 423.012177u**
**Observed Mass = 423.012392u**
**Difference = < 1.0 ppm**




| m/z | I |
|---|---|
| 208.398141 | 5751105 |
| 215.089161 | 8268868 |
| 288.289858 | 17828588 |
| 289.293252 | 2935542 |
| 316.321243 | 13452327 |
| 360.323906 | 3321452 |
| 393.297819 | 3065399 |
| 399.014810 | 11767943 |
| 401.012741 | 12001442 |
| 403.009820 | 3757246 |
| 413.264319 | 4925770 |
| 413.265301 | 12126538 |
| 413.266250 | 206383434 |
| 413.267128 | 17942858 |
| 413.267654 | 7678282 |
| 413.268144 | 4202826 |
| 414.268825 | 4233560 |
| 414.269696 | 46999896 |
| 415.273221 | 4471142 |
| 419.277049 | 5893532 |
| 423.012392 | 9392590 |

| m/z | I |
|---|---|
| 425.010368 | 8980968 |
| 425.287650 | 6170092 |
| 427.007503 | 3044354 |
| 427.245801 | 2966022 |
| 429.240443 | 7027232 |
| 430.389371 | 8854063 |
| 433.241119 | 4847188 |
| 435.202766 | 10297965 |
| 435.344727 | 13228655 |
| 436.348153 | 3180156 |
| 437.193663 | 26684039 |
| 438.197140 | 6017683 |
| 441.297608 | 103738043 |
| 442.301074 | 25774791 |
| 452.482879 | 4122437 |
| 455.313444 | 3660646 |
| 457.271663 | 4097918 |
| 463.197653 | 7023554 |
| 463.303171 | 25963459 |
| 464.306648 | 5885903 |
| 469.329074 | 14646279 |
| 470.332456 | 3858450 |
| 477.267309 | 7367772 |
| 479.228856 | 48835697 |
| 479.230031 | 4244593 |
| 480.228613 | 5833851 |
| 480.232349 | 7500923 |
| 481.225862 | 3845253 |
| 507.223903 | 6497658 |
| 507.329327 | 48000379 |
| 507.330619 | 4089211 |
| 508.332823 | 12778884 |
| 521.293542 | 6303214 |
| 523.254906 | 73723390 |
| 524.254779 | 8791558 |
| 524.258472 | 13360646 |
| 525.252060 | 5584397 |
| 540.426201 | 6254205 |
| 548.467656 | 3797684 |
| 550.628796 | 4430530 |
| 551.355531 | 61468359 |
| 551.357174 | 4183751 |
| 552.358967 | 17288910 |
| 553.459411 | 6366933 |
| 565.319815 | 4637471 |
| 567.279335 | 4337451 |
| 567.281126 | 78491435 |
| 567.282885 | 6008619 |
| 568.281046 | 9307953 |
| 568.284715 | 15753009 |
| 569.278340 | 6010679 |
| 569.381516 | 3144504 |
| 593.402628 | 3635134 |
| 595.381667 | 49901512 |
| 596.385269 | 14442445 |
| 611.305322 | 3694616 |
| 611.307330 | 48230424 |
| 611.309397 | 3571736 |
| 612.307145 | 4992029 |
| 612.310840 | 10190877 |
| 613.304394 | 3330082 |

| m/z | I |
|---|---|
| 639.407998 | 27431059 |
| 640.411486 | 7897238 |
| 655.333656 | 24965323 |
| 656.337218 | 6080719 |
| 683.434196 | 10510612 |
| 684.437560 | 3668246 |
| 685.435563 | 35377432 |
| 686.439093 | 13955354 |
| 699.359857 | 11374892 |
| 700.363283 | 2990381 |
| 727.460261 | 3209522 |
| 743.386064 | 3986727 |
| 803.543189 | 24523072 |
| 804.546522 | 11600195 |
| 831.574507 | 14066126 |
| 832.577851 | 7604694 |
| 859.605678 | 3839720 |
| 877.535089 | 4178900 |



**38c-1**

Chemical Formula: $C_{24}H_{26}O$

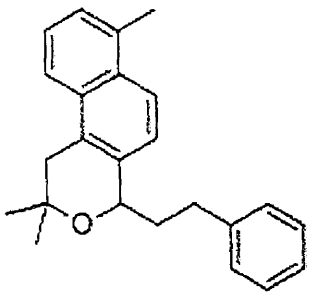
Molecular Weight: 330.47




| | | | | |
|---|---|---|---|---|
| PULSE SEQUENCE<br>Relax. delay 1.000 sec<br>Pulse 14.8 degrees<br>Acq. time 1.998 sec<br>Width 6402.0 Hz<br>32 repetitions | OBSERVE H1, 399.8398946 | DATA PROCESSING<br>Line broadening 1.0 Hz<br>FT size 32768<br>Total time 1 minutes | | YC-187 pure pdt;<br>mono-methyl-sub.<br>alkynediol with<br>phenylpropionaldehyde to<br>form tricyclic<br>isochromenes; cdcl3;<br>7/20/2014<br>~~Eehpen80 (CDCl3 293.1 K~~ |

YC-187 pure pdt; mono-methyl-sub. alkynediol with phenylpropionaldehyde to form tricyclic isochromenes; cdcl3; 7/20/2014

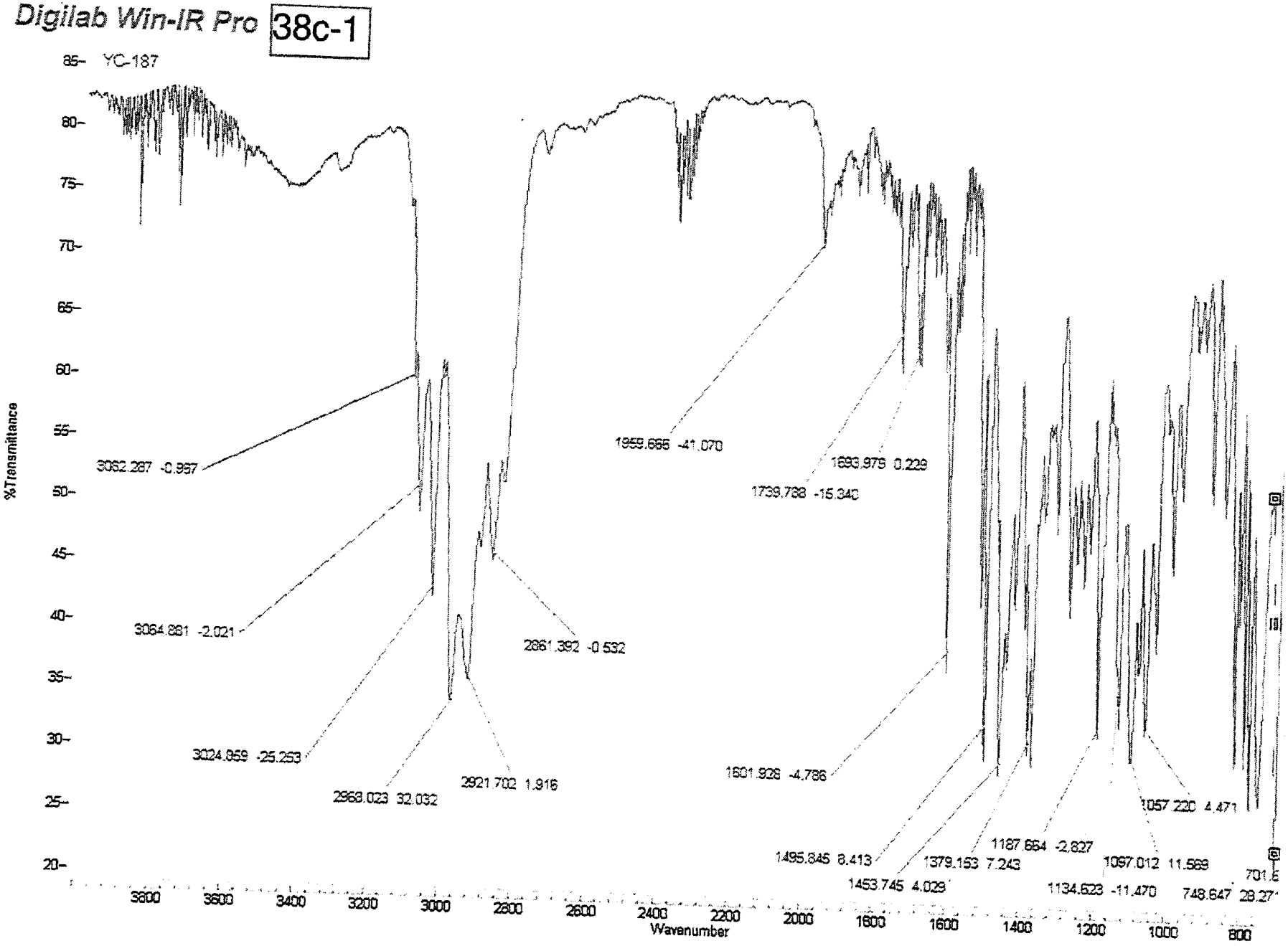
Sample Name:
yc-187



**38c-1**

Chemical Formula: $C_{24}H_{26}O$

Molecular Weight: 330.47


Digilab Win-IR Pro
38c-1
YC-187
%Transmittance
Wavenumber
3062.287 -0.997
3024.869 -25.253
2968.023 32.032
2921.702 1.916
2861.392 -0.532
1959.666 -41.070
1739.788 -15.340
1693.979 0.229
1601.926 -4.786
1495.845 8.413
1453.745 4.029
1379.153 7.243
1187.664 -2.827
1134.623 -11.470
1097.012 11.589
1057.220 4.471
748.647 28.27

# Mass Spectrum List Report

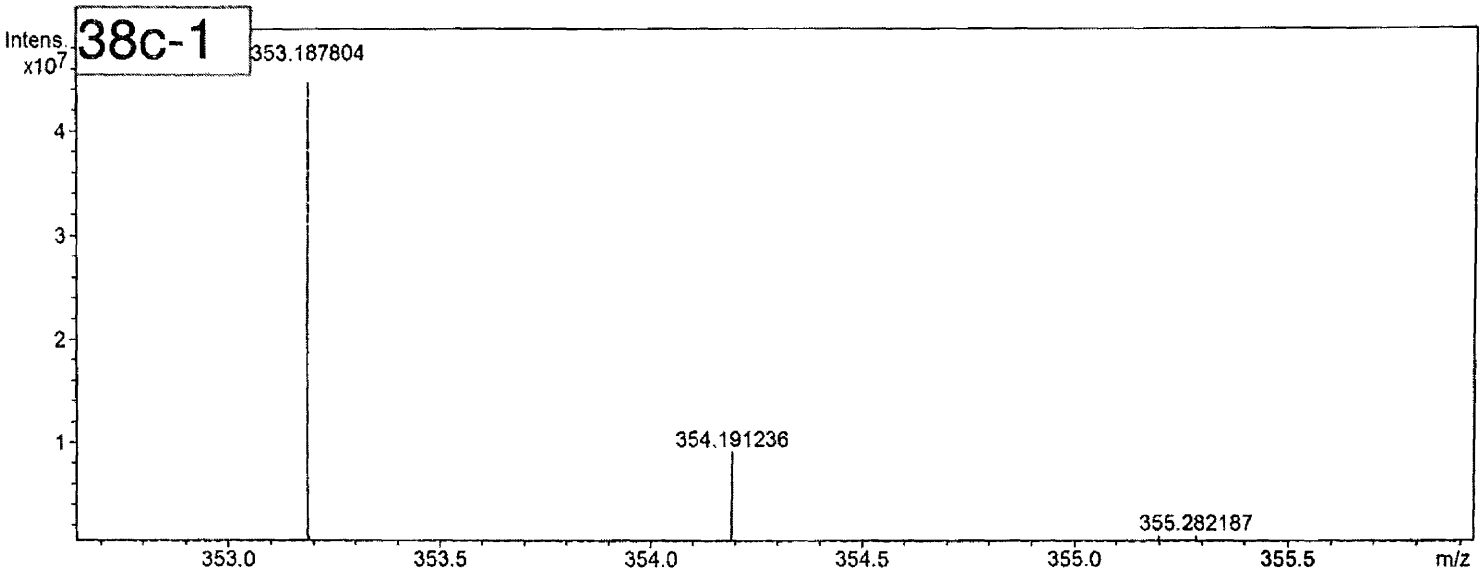


**Analysis Info**

| | | | |
|---|---|---|---|
| Analysis Name | YC-187_pos_000001.d | Acquisition Date | 7/22/2014 4:15:13 PM |
| Method | XMASS_Method | Operator | FTMS_USER |
| Sample Name: | YC-187_pos | Instrument | apex-Qe |
| | YC-187_pos: in 1:1 THF:MeOH w/ NaCl.. | | |

**Acquisition Parameter**

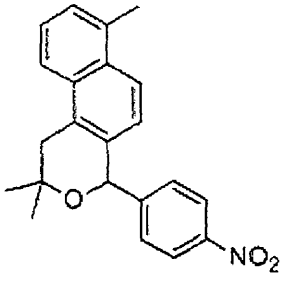
**Sample: YC-187**
**Exact Mass of = (C24H26O)Na+ : 353.187587u**
**Observed Mass = 353.187804u**
**Difference = < 1.0 ppm**




| m/z | I |
|---|---|
| 174.370852 | 4190871 |
| 192.463079 | 3839788 |
| 288.288604 | 12192727 |
| 288.289278 | 19383255 |
| 288.289801 | 202580951 |
| 288.290478 | 8297431 |
| 288.290724 | 5051351 |
| 289.292080 | 3492325 |
| 289.293299 | 12465125 |
| 304.284858 | 17153212 |
| 316.320298 | 41473384 |
| 316.320523 | 43271528 |
| 316.321073 | 287483240 |
| 316.321822 | 12039529 |
| 316.322114 | 7073129 |
| 316.322405 | 4598121 |
| 317.323588 | 8405623 |
| 317.324599 | 28767607 |
| 318.328014 | 4498309 |
| 329.190309 | 5220890 |
| 332.315531 | 4225603 |

| m/z | I |
|---|---|
| 332.316145 | 37238339 |
| 333.319589 | 5496400 |
| 338.303244 | 3423375 |
| 353.187804 | 46122807 |
| 354.191236 | 9088833 |
| 360.324021 | 4731772 |
| 360.347525 | 6081404 |
| 366.278928 | 4050864 |
| 372.347552 | 6517729 |
| 375.250924 | 4323319 |
| 388.543439 | 6277201 |
| 399.250935 | 7354512 |
| 413.266549 | 28846299 |
| 414.269975 | 5817568 |
| 419.277145 | 23996665 |
| 420.280513 | 4336895 |
| 425.287748 | 4390168 |
| 433.241198 | 3606850 |
| 435.202872 | 5184844 |
| 435.344886 | 5773645 |
| 437.192164 | 4870487 |
| 437.193628 | 139831639 |
| 438.196215 | 3549532 |
| 438.197131 | 32155996 |
| 441.297933 | 12753261 |
| 442.301311 | 3343731 |
| 447.229766 | 43461008 |
| 447.230850 | 3572112 |
| 448.233215 | 11934102 |
| 452.482959 | 3527088 |
| 453.167775 | 15776180 |
| 454.171214 | 3464635 |
| 463.302197 | 4358649 |
| 463.303344 | 54159865 |
| 463.304514 | 4139513 |
| 464.306800 | 12024320 |
| 477.267465 | 3787368 |
| 479.229057 | 35449466 |
| 480.228727 | 3953283 |
| 480.232480 | 5188227 |
| 495.266312 | 10736405 |
| 507.224061 | 4261780 |
| 507.329523 | 71379861 |
| 508.333039 | 16505760 |
| 523.255297 | 40102981 |
| 524.254956 | 4556881 |
| 524.258719 | 6544465 |
| 540.426256 | 26053892 |
| 541.429709 | 6778127 |
| 548.467746 | 15932762 |
| 549.471153 | 5116261 |
| 551.355715 | 78720377 |
| 551.357271 | 6892921 |
| 552.359203 | 20499843 |
| 554.551185 | 4649370 |
| 567.279894 | 3698197 |
| 567.281511 | 43593237 |
| 568.281166 | 4712990 |
| 568.284955 | 7960094 |
| 568.457556 | 9387551 |
| 576.499060 | 5173860 |

| m/z | I |
|---|---|
| 595.381910 | 57994983 |
| 595.383783 | 4808423 |
| 596.385442 | 14622444 |
| 605.490304 | 4461336 |
| 611.307768 | 16662317 |
| 612.311168 | 3480369 |
| 639.408331 | 26226533 |
| 640.411692 | 7446373 |
| 653.342747 | 3941227 |
| 655.334042 | 8931179 |
| 683.434481 | 12656488 |
| 684.437880 | 4273000 |
| 685.432123 | 4284264 |
| 685.435665 | 116502376 |
| 686.439252 | 46903144 |
| 687.442765 | 6506345 |
| 699.360303 | 5006189 |
| 727.460686 | 4892574 |



**38c-2**

Chemical Formula: $C_{22}H_{21}NO_3$

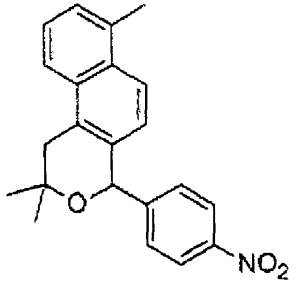
Molecular Weight: 347.41




| | | | | |
|---|---|---|---|---|
| PULSE SEQUENCE<br>Relax. delay 1.000 sec<br>Pulse 5.0 degrees<br>Acq. time 1.998 sec<br>Width 6402.0 Hz<br>16 repetitions | OBSERVE H1, 399.8398946 | DATA PROCESSING<br>FT size 32768<br>Total time 1 minute | | YC-186 pure; mono-methyl sub. diol with p-nitro-benzaldehyde to form tricyclic isochromenes; cdcl3; 7/17/2014<br>Solvent: cdcl3 293.1 K |

YC-186 pure; mono-methyl sub. diol with p-nitro-benzaldehyde to form tricyclic isochromenes; cdcl3; 7/17/2014

Sample Name:
YC-184-pdt

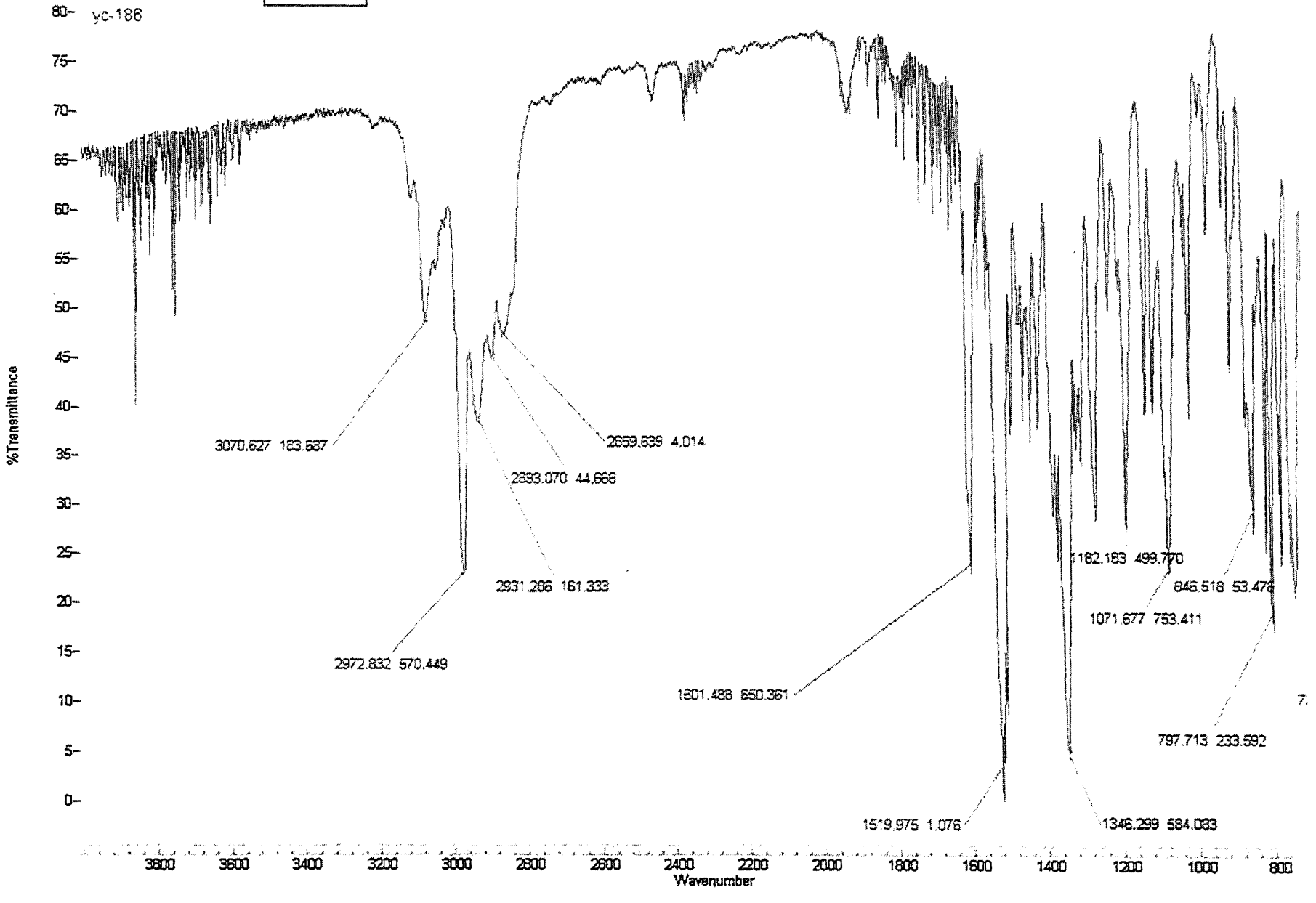


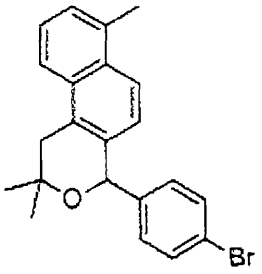

**38c-2**

Chemical Formula: $C_{22}H_{21}NO_3$

Molecular Weight: 347.41

Digilab Win-IR Pro 38c-2

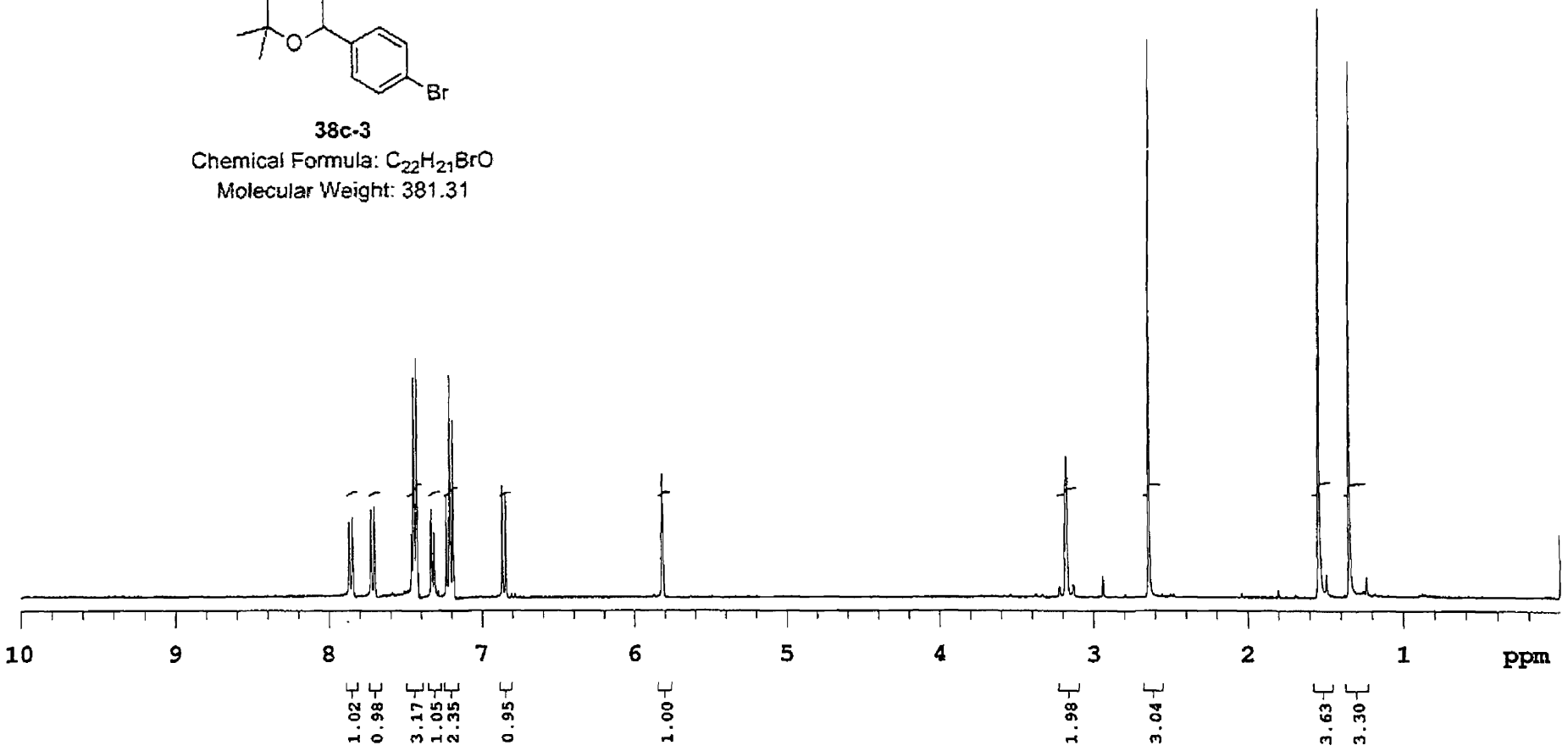





**38c-3**

Chemical Formula: $C_{22}H_{21}BrO$

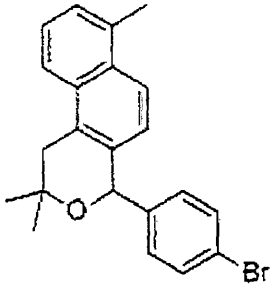
Molecular Weight: 381.31




| | | | | |
|---|---|---|---|---|
| PULSE SEQUENCE<br>Relax. delay 1.000 sec<br>Pulse 5.0 degrees<br>Acq. time 1.998 sec<br>Width 6402.0 Hz<br>16 repetitions | OBSERVE H1, 399.8398981 | DATA PROCESSING<br>FT size 32768<br>Total time 1 minute | | YC-184 pure pdt;<br>mono-methyl sub. diol<br>with 4-bromo-benzaldehyde<br>to form tricyclic<br>isochromene; cdcl3;<br>6/8/2014<br>Solvent cdcl3 293.1 K |

YC-184 pure pdt; mono-methyl sub. diol with 4-bromo-benzaldehyde to form tricyclic isochromene; cdcl3; 6/8/2014

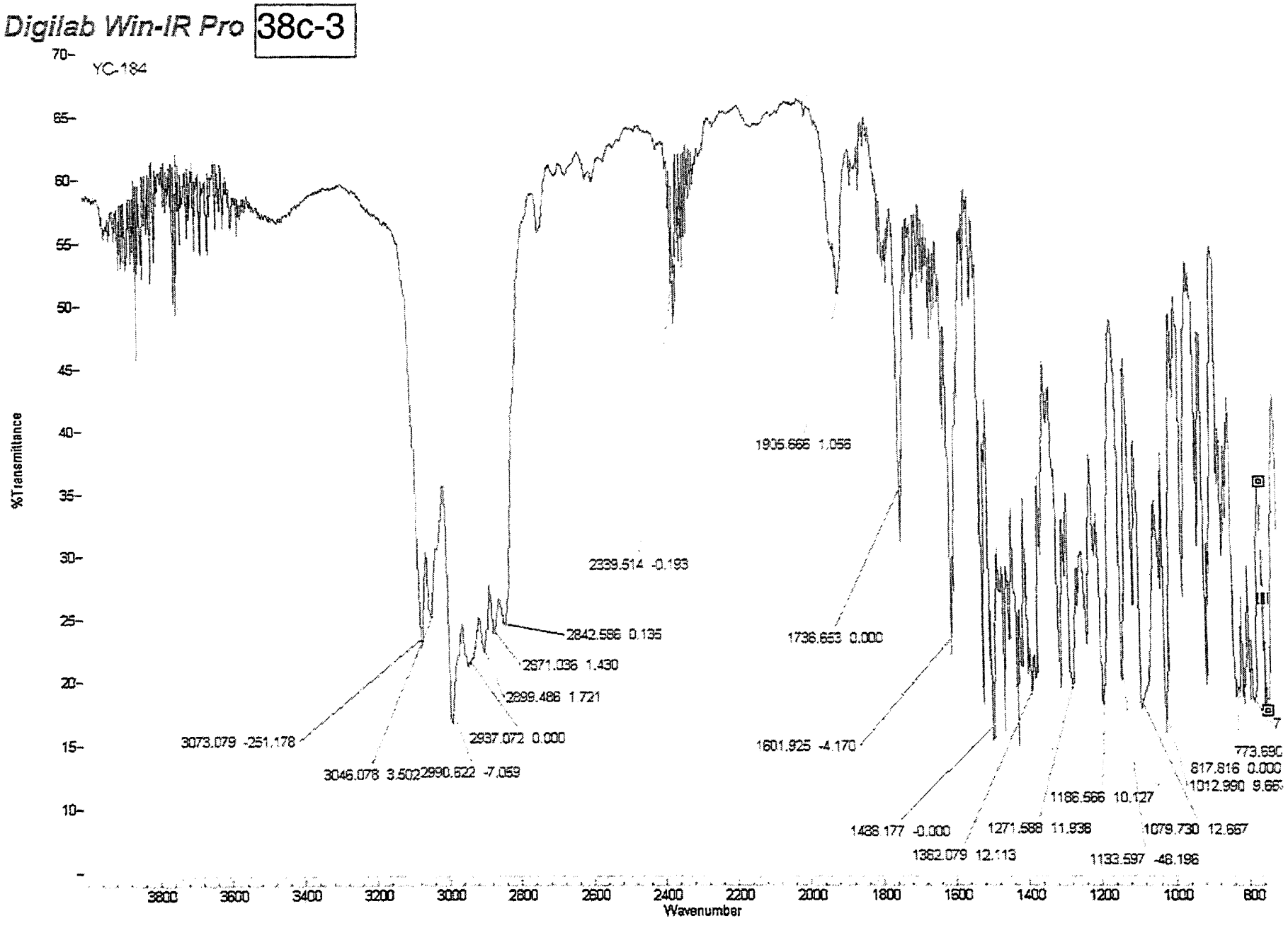
Sample Name:
yc-184

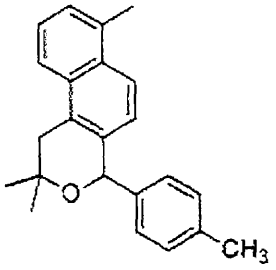



**38c-3**

Chemical Formula: $C_{22}H_{21}BrO$

Molecular Weight: 381.31


Digilab Win-IR Pro
38c-3
YC-184
%Transmittance
Wavenumber
3073.079 -251.178
3046.078 3.502
2990.622 -7.059
2937.072 0.000
2899.486 1.721
2871.036 1.430
2842.586 0.135
2339.514 -0.193
1905.666 1.056
1736.653 0.000
1601.925 -4.170
1488.177 -0.000
1382.079 12.113
1271.588 11.938
1186.566 10.127
1133.597 -46.196
1079.730 12.667
1012.990 9.65
817.816 0.000
773.690



**38c-4**

Chemical Formula: $C_{23}H_{24}O$

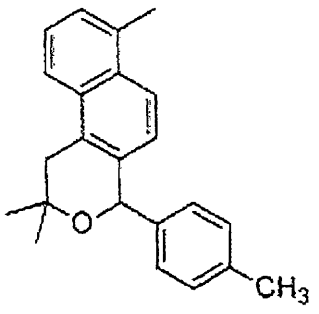
Molecular Weight: 316.44




| | | | | |
|---|---|---|---|---|
| PULSE SEQUENCE<br>Relax. delay 1.000 sec<br>Pulse 14.8 degrees<br>Acq. time 1.998 sec<br>Width 6402.0 Hz<br>4 repetitions | OBSERVE H1, 399.8399020 | DATA PROCESSING<br>FT size 32768<br>Total time 1 minute | | YC-185 pure; mono-methyl sub. diol with p-tolualdehyde to form tricyclic isochromenes; cdcl3; 7/17/2014<br>Solvent: CDCl3<br>Temp. 20.0 C / 293.1 K |

YC-185 pure pdt; mono-methyl sub. diol with 4-methyl-benzaldehyde to form tricyclic isochromene; cdcl3; 6/8/2014

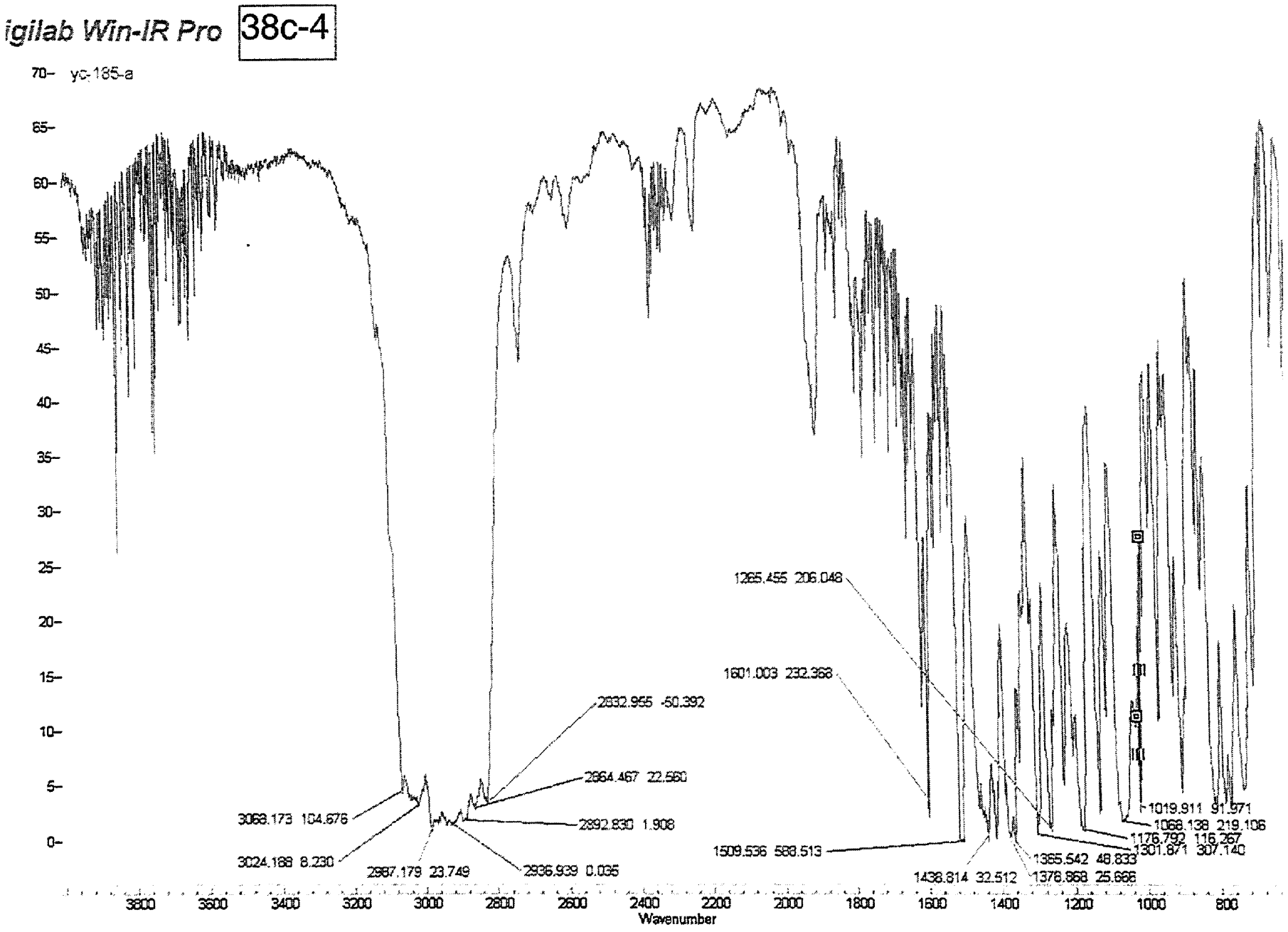
Sample Name:
YC-185-pdt




**38c-4**

Chemical Formula: $C_{23}H_{24}O$

Molecular Weight: 316.44


igilab Win-IR Pro
38c-4
yc-185-a
70
65
60
55
50
45
40
35
30
25
20
15
10
5
0
3068.173 104.676
3024.188 8.230
2987.179 23.749
2936.939 0.035
2892.830 1.908
2864.467 22.560
2832.955 -50.392
1601.003 232.368
1265.455 206.048
1509.536 588.513
1438.814 32.512
1376.868 25.666
1365.542 48.833
1301.871 307.140
1176.792 116.267
1068.138 219.106
1019.911 91.971
3800
3600
3400
3200
3000
2800
2600
2400
2200
2000
1800
1600
1400
1200
1000
800
Wavenumber

# Mass Spectrum List Report

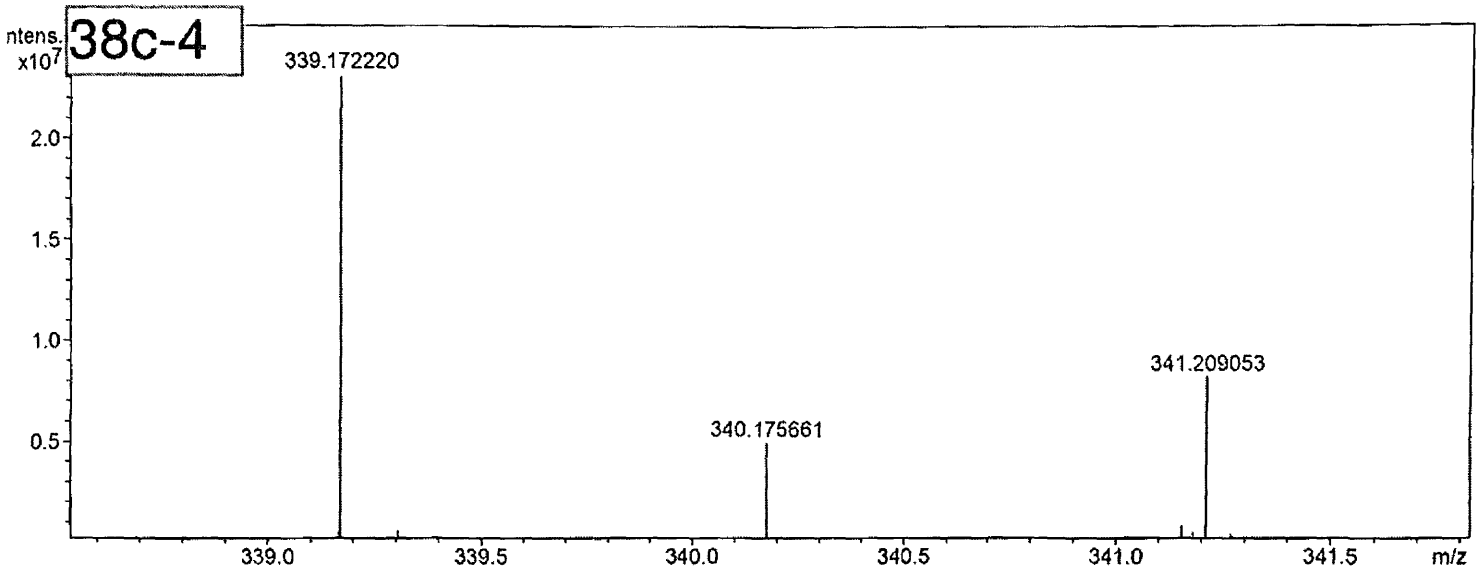


**Analysis Info**

| | | | |
|---|---|---|---|
| Analysis Name | YC-185_pos_000001.d | Acquisition Date | 7/22/2014 4:08:48 PM |
| Method | XMASS_Method | Operator | FTMS_USER |
| Sample Name: | YC-185_pos | Instrument | apex-Qe |
| | YC-185_pos: in 1:1 THF:MeOH w/ NaCl.. | | |

**Acquisition Parameter**

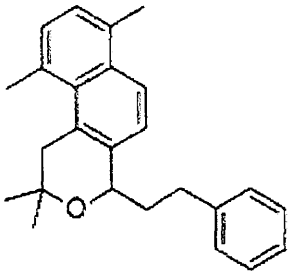
**Sample: YC-183**
**Exact Mass of = (C23H24O)Na+ : 339.171936u**
**Observed Mass = 339.172220u**
**Difference = < 1.0 ppm**




| m/z | I |
|---|---|
| 192.463085 | 6897427 |
| 288.288646 | 7973777 |
| 288.289340 | 12082065 |
| 288.289801 | 203465617 |
| 288.290232 | 19886993 |
| 288.290473 | 8908689 |
| 288.290726 | 4899729 |
| 289.293279 | 30782366 |
| 299.178593 | 4072863 |
| 299.178891 | 3778079 |
| 299.179633 | 35845151 |
| 300.183052 | 8233004 |
| 304.284886 | 17083491 |
| 315.174654 | 4883189 |
| 316.320273 | 35304709 |
| 316.320561 | 32789765 |
| 316.321070 | 301737221 |
| 316.321815 | 12866821 |
| 316.322103 | 7452933 |
| 316.322403 | 4715781 |
| 317.323534 | 6676114 |

| m/z | I |
|---|---|
| 317.324596 | 43533586 |
| 318.328065 | 4292896 |
| 332.316173 | 35190233 |
| 333.319616 | 5481958 |
| 337.235244 | 13807128 |
| 339.172220 | 23156272 |
| 340.175661 | 4953660 |
| 341.209053 | 8212041 |
| 343.188314 | 5440097 |
| 355.167197 | 4307693 |
| 360.347550 | 5354277 |
| 375.250965 | 4907960 |
| 381.260831 | 5216239 |
| 381.261484 | 27883503 |
| 382.264912 | 4695032 |
| 388.543442 | 6748206 |
| 399.250156 | 3788932 |
| 399.250908 | 20048004 |
| 400.254341 | 4787340 |
| 413.266533 | 50391276 |
| 413.267364 | 4753644 |
| 414.270005 | 9674995 |
| 419.277189 | 23374102 |
| 420.280573 | 4467997 |
| 425.287793 | 4934974 |
| 435.344947 | 6253952 |
| 437.193617 | 241150348 |
| 438.196171 | 5622162 |
| 438.197130 | 58255762 |
| 439.200612 | 4670873 |
| 439.203686 | 7188889 |
| 441.298001 | 3772838 |
| 453.166695 | 4624881 |
| 453.167740 | 48753137 |
| 454.171224 | 9863671 |
| 463.302260 | 4205104 |
| 463.303392 | 52079152 |
| 463.304545 | 4424240 |
| 464.306864 | 11350582 |
| 479.229123 | 29919893 |
| 480.232535 | 4465307 |
| 491.219794 | 8454883 |
| 495.266341 | 13560573 |
| 507.328247 | 5905229 |
| 507.329579 | 76524365 |
| 507.330994 | 5425997 |
| 508.333093 | 18623316 |
| 523.255387 | 33369014 |
| 524.258815 | 5304253 |
| 540.426350 | 15117350 |
| 541.429794 | 4396076 |
| 548.467834 | 12119129 |
| 549.471167 | 4196447 |
| 551.355786 | 80866411 |
| 552.359282 | 20262002 |
| 554.551250 | 4253823 |
| 561.397896 | 6978729 |
| 567.281622 | 35179725 |
| 568.285059 | 6153427 |
| 568.457651 | 6397140 |
| 576.499157 | 4427010 |

| m/z | I |
|---|---|
| 595.382003 | 55930217 |
| 596.385557 | 13503854 |
| 605.490217 | 4603291 |
| 611.307862 | 13827511 |
| 619.439728 | 7925212 |
| 639.408428 | 26955314 |
| 640.411805 | 7394870 |
| 655.334222 | 6098547 |
| 677.481683 | 6424268 |
| 683.434661 | 11042532 |
| 685.432161 | 5588717 |
| 685.435659 | 162246381 |
| 686.439299 | 63581937 |
| 687.442968 | 8462069 |
| 701.410139 | 5143345 |
| 727.460807 | 5171115 |
| 735.523621 | 5703636 |
| 793.565374 | 4003127 |



**38d-1**

Chemical Formula: $C_{25}H_{28}O$

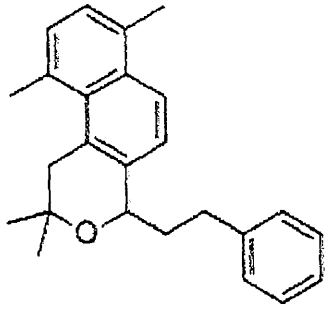
Molecular Weight: 344.50




| | | | | |
|---|---|---|---|---|
| PULSE SEQUENCE<br>Relax. delay 1.000 sec<br>Pulse 45.0 degrees<br>Acq. time 2.556 sec<br>Width 6410.3 Hz<br>4 repetitions | OBSERVE H1, 399.8398982 | DATA PROCESSING<br>FT size 32768<br>Total time 1 minute | | YC-192 pure pdt;<br>2,5-dimethyl-diol with phenylpropionaldehyde to form tricyclic isochromene; cdcl3;<br>6/19/2014<br>Solvent: cdcl3<br>Ambient temperature |

YC-192 pure pdt; 2,5-dimethyl-diol with phenylpropionaldehyde to form tricyclic isochromene; cdcl3; 6/19/2014

Sample Name:
YC-192-14-22

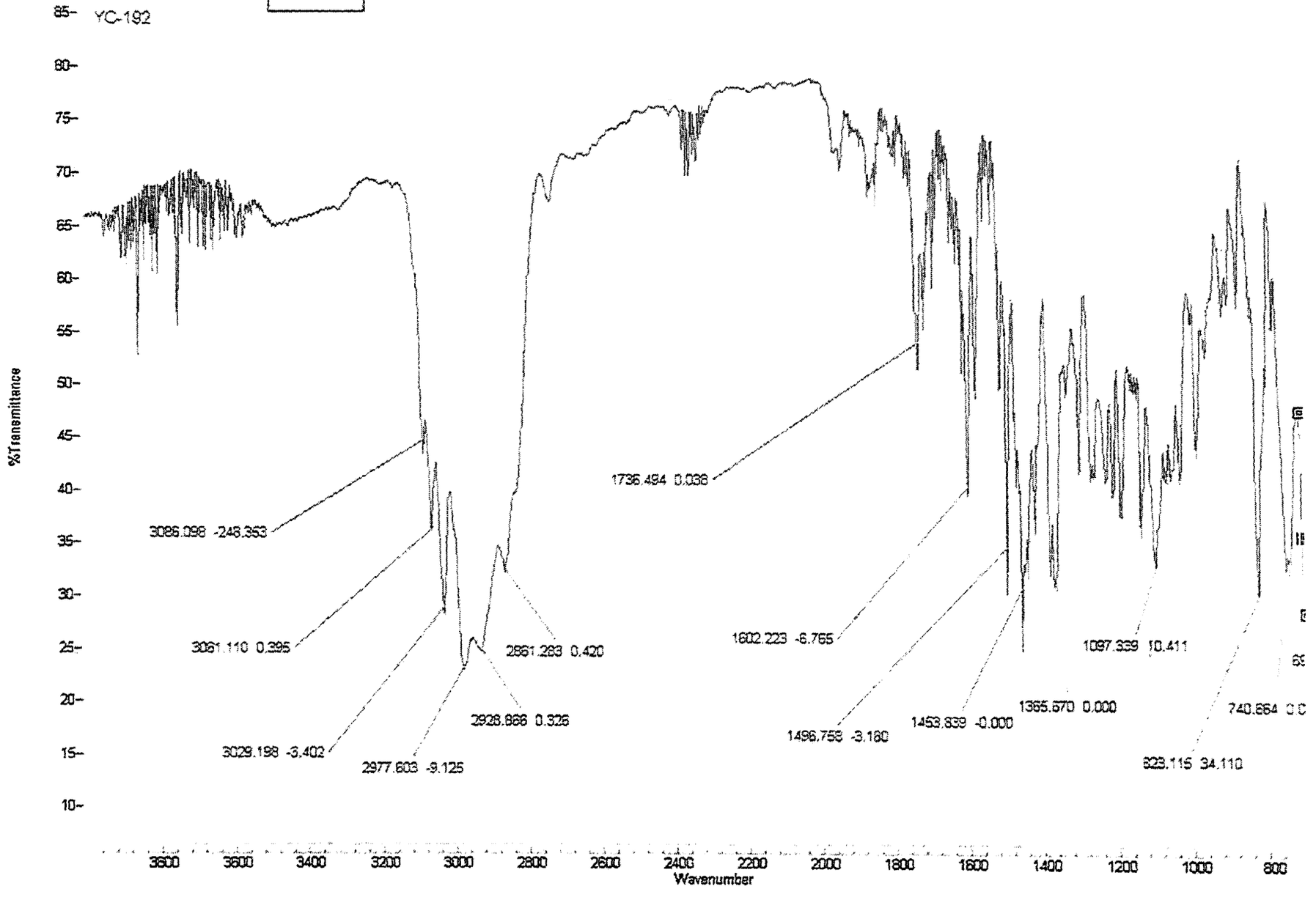


**38d-1**

Chemical Formula: $C_{25}H_{28}O$

Molecular Weight: 344.50

Digilab Win-IR Pro 38d-1



# Mass Spectrum List Report

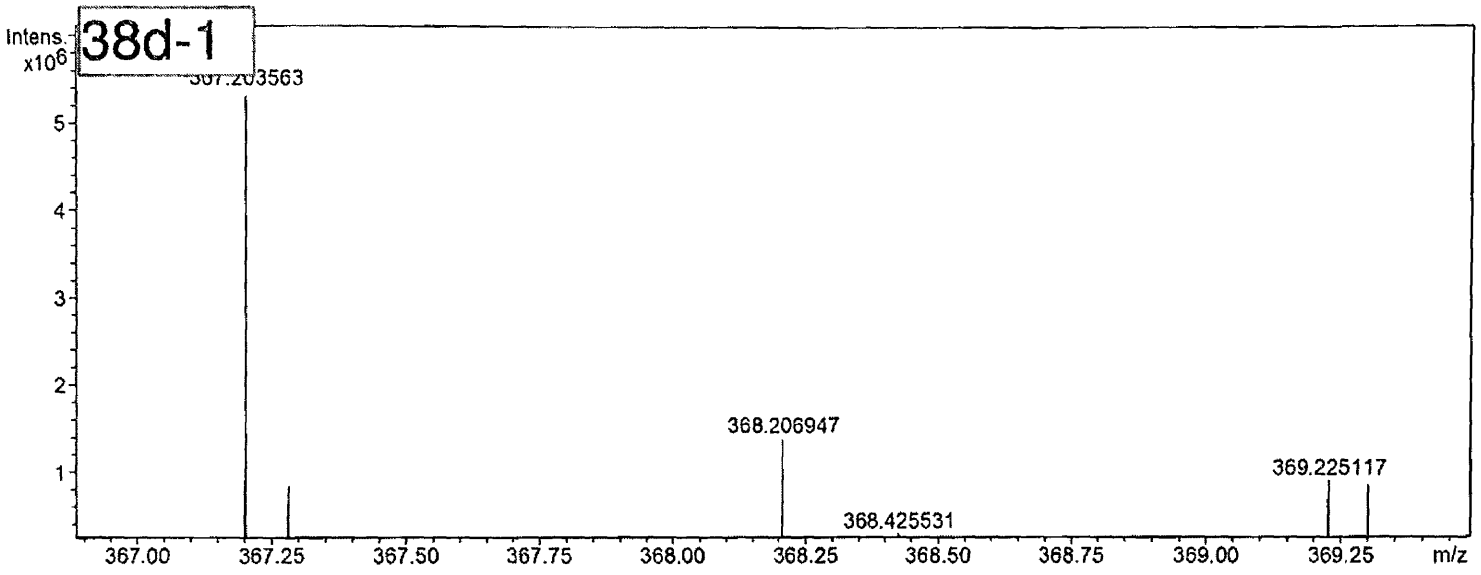


**Analysis Info**

| | | | |
|---|---|---|---|
| Analysis Name | YC-192_pos_000001.d | Acquisition Date | 7/22/2014 4:30:02 PM |
| Method | XMASS_Method | Operator | FTMS_USER |
| Sample Name: | YC-192_pos | Instrument | apex-Qe |
| | YC-192_pos: In 1:1 THF:MeOH w/ NaCl.. | | |

**Acquisition Parameter**

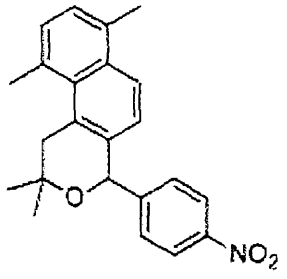
**Sample: YC-192**
**Exact Mass of = (C25H28O)Na+ : 367.203237u**
**Observed Mass = 367.203563u**
**Difference = < 1.0 ppm**




| m/z | I |
|---|---|
| 174.370848 | 5357294 |
| 277.120126 | 3642895 |
| 288.288532 | 15253408 |
| 288.289049 | 16864160 |
| 288.289359 | 16417696 |
| 288.289782 | 255402912 |
| 288.290460 | 9342880 |
| 288.290960 | 3686304 |
| 289.292071 | 6655405 |
| 289.293249 | 42795949 |
| 290.296675 | 3594170 |
| 304.284853 | 28968059 |
| 305.157342 | 4686983 |
| 305.288243 | 3664521 |
| 316.305527 | 3644195 |
| 316.313262 | 4762403 |
| 316.320052 | 35728675 |
| 316.321062 | 340796707 |
| 316.321811 | 14632227 |
| 316.322114 | 8592675 |
| 316.322405 | 5777699 |

| m/z | I |
|---|---|
| 316.322702 | 4106019 |
| 317.323474 | 6922033 |
| 317.323953 | 5382449 |
| 317.324550 | 60712241 |
| 318.328026 | 3639103 |
| 332.316131 | 51291646 |
| 333.319572 | 8011275 |
| 338.303257 | 4888652 |
| 341.190290 | 3960944 |
| 343.205947 | 6197897 |
| 349.183588 | 3848913 |
| 360.347524 | 6908748 |
| 366.278933 | 4665225 |
| 367.203563 | 5359506 |
| 372.347560 | 3822019 |
| 375.250926 | 5678045 |
| 381.182843 | 9642002 |
| 381.261505 | 7133202 |
| 388.543437 | 5983311 |
| 413.266601 | 12024070 |
| 419.277129 | 31877423 |
| 420.280526 | 5998901 |
| 425.287730 | 4919638 |
| 435.202883 | 5134743 |
| 435.344885 | 6010264 |
| 437.192136 | 4014500 |
| 437.193689 | 104180132 |
| 438.197173 | 21965227 |
| 441.297928 | 5350847 |
| 453.167779 | 7236109 |
| 461.245533 | 5279300 |
| 463.302185 | 4860498 |
| 463.303340 | 63482450 |
| 463.304529 | 4659794 |
| 464.306796 | 14891609 |
| 477.267460 | 3641016 |
| 479.229078 | 34867910 |
| 480.228729 | 4046542 |
| 480.232486 | 5386958 |
| 507.224058 | 4369320 |
| 507.328305 | 7248809 |
| 507.329534 | 87337897 |
| 508.333035 | 22096818 |
| 523.255331 | 40438831 |
| 524.254954 | 4945976 |
| 524.258755 | 6845496 |
| 540.426299 | 19070142 |
| 541.429717 | 5397702 |
| 548.467782 | 13470975 |
| 549.471158 | 4593927 |
| 551.355722 | 97299734 |
| 551.357265 | 8097046 |
| 552.359219 | 25996573 |
| 554.551168 | 5194030 |
| 564.462682 | 4240761 |
| 565.371605 | 3638656 |
| 567.279886 | 3624334 |
| 567.281543 | 44739982 |
| 568.281223 | 5120405 |
| 568.284960 | 7884181 |
| 568.457600 | 8103318 |

| m/z | I |
|---|---|
| 576.499103 | 5230030 |
| 595.381923 | 68546112 |
| 595.383774 | 5684800 |
| 596.385464 | 18005573 |
| 605.490522 | 5131890 |
| 611.307819 | 17055372 |
| 612.311232 | 3837584 |
| 639.408343 | 35106538 |
| 640.411761 | 9686764 |
| 655.334085 | 8625931 |
| 683.434585 | 16817964 |
| 684.437986 | 5498668 |
| 685.432023 | 4132653 |
| 685.435786 | 117157677 |
| 686.439381 | 46018349 |
| 687.442936 | 7001902 |
| 699.360403 | 4753202 |
| 727.460805 | 7231281 |



**38d-2**

Chemical Formula: $C_{23}H_{23}NO_3$

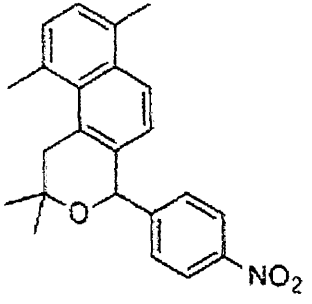
Molecular Weight: 361.44




| | | | | |
|---|---|---|---|---|
| PULSE SEQUENCE<br>Relax. delay 1.000 sec<br>Pulse 45.0 degrees<br>Acq. time 2.556 sec<br>Width 6410.3 Hz<br>4 repetitions | OBSERVE H1, 399.8398939 | DATA PROCESSING<br>FT size 32768<br>Total time 1 minute | | YC-191 pure pdt;<br>2,5-dimethyl-diol with p-nitro-benzaldehyde to form tricyclic isochromene; cdcl3;<br>6/19/2014<br>184<br>Solvent : cdcl3 Temperature |

YC-191 pure pdt; 2,5-dimethyl-diol with 4-nitro-benzaldehyde to form tricyclic isochromene; cdcl3; 6/16/2014

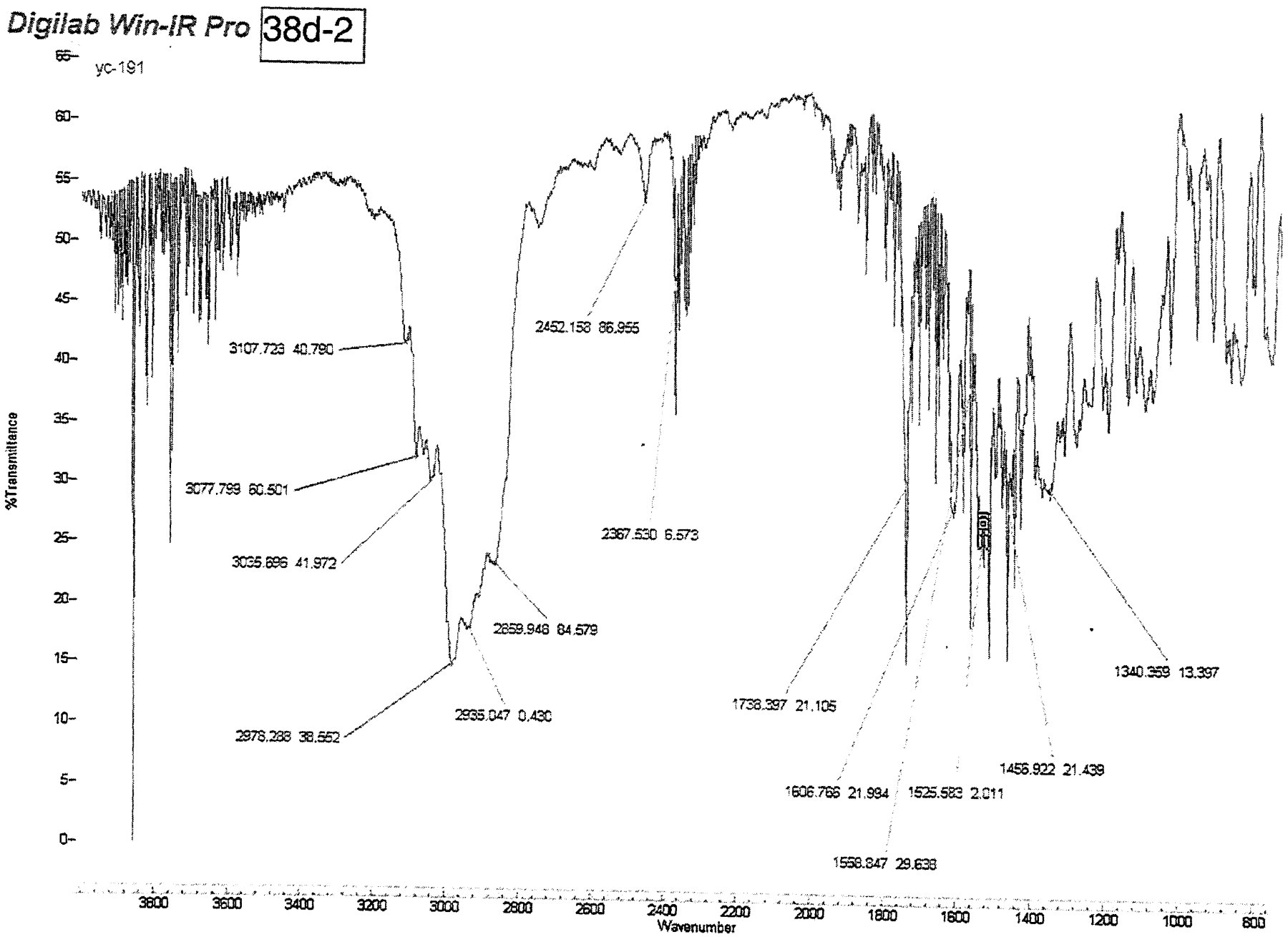
Sample Name:
yc-191




**38d-2**

Chemical Formula: $C_{23}H_{23}NO_3$

Molecular Weight: 361.44


Digilab Win-IR Pro
38d-2
yc-191
%Transmittance
Wavenumber
3107.723 40.790
3077.799 60.501
3036.696 41.972
2978.288 38.552
2935.047 0.430
2859.946 84.579
2452.158 86.955
2367.530 6.573
1738.397 21.105
1606.766 21.984
1558.847 29.638
1525.583 2.011
1456.922 21.439
1340.359 13.397

# Mass Spectrum List Report

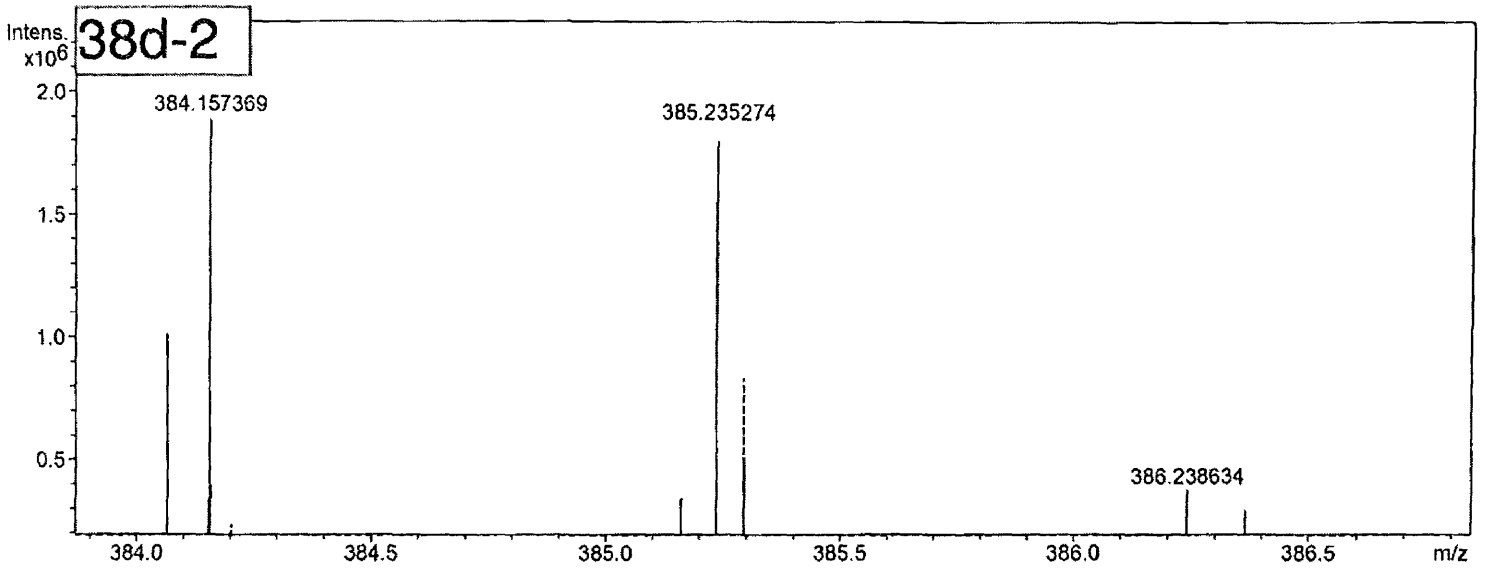


**Analysis Info**

| | | | |
|---|---|---|---|
| Analysis Name | YC-191_pos_000001.d | Acquisition Date | 7/22/2014 4:26:17 PM |
| Method | XMASS_Method | Operator | FTMS_USER |
| Sample Name: | YC-191_pos | Instrument | apex-Qe |
| | YC-191_pos: in 1:1 THF:MeOH w/ NaCl.. | | |

**Acquisition Parameter**

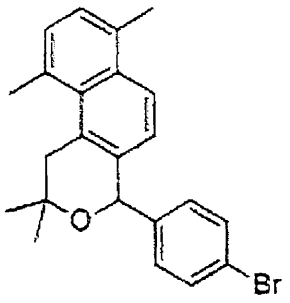
**Sample: YC-191**
**Exact Mass of = (C23H23NO3)Na+ : 384.157015u**
**Observed Mass = 384.157369u**
**Difference = < 1.0 ppm**




| m/z | I |
|---|---|
| 220.086169 | 3404787 |
| 255.135761 | 3352589 |
| 288.287888 | 3661827 |
| 288.288576 | 9949187 |
| 288.289054 | 19055619 |
| 288.289800 | 204301315 |
| 288.290527 | 9964547 |
| 288.291045 | 4139011 |
| 289.292075 | 2912276 |
| 289.293299 | 13190164 |
| 304.284861 | 18339095 |
| 316.318762 | 3816935 |
| 316.320255 | 34055655 |
| 316.320573 | 24219111 |
| 316.321075 | 267232743 |
| 316.321889 | 11587047 |
| 316.322662 | 5017063 |
| 316.323271 | 3311079 |
| 317.323589 | 6779384 |
| 317.324587 | 39732728 |
| 318.328041 | 4658697 |

| m/z | I |
|---|---|
| 327.193364 | 9554587 |
| 332.316146 | 40740588 |
| 333.319597 | 7087867 |
| 337.235228 | 11065142 |
| 338.303248 | 6036294 |
| 352.282539 | 3710465 |
| 360.324012 | 12580955 |
| 360.347525 | 4742236 |
| 366.278935 | 5960855 |
| 372.347563 | 5711054 |
| 375.250955 | 3892966 |
| 381.261440 | 30271764 |
| 382.264882 | 5215516 |
| 388.543417 | 6337862 |
| 399.249049 | 4295045 |
| 399.250745 | 123808133 |
| 399.252230 | 4220293 |
| 400.254274 | 26171787 |
| 400.378881 | 3182987 |
| 408.232604 | 4080050 |
| 413.266588 | 18729417 |
| 414.270002 | 4113870 |
| 419.240828 | 2948067 |
| 419.277138 | 23005667 |
| 420.280534 | 4523495 |
| 421.233002 | 3430891 |
| 425.287730 | 7303675 |
| 435.202903 | 4911649 |
| 435.344899 | 8245794 |
| 437.192055 | 3600937 |
| 437.193689 | 75655721 |
| 438.197169 | 16276013 |
| 441.297944 | 10531384 |
| 463.303352 | 43879060 |
| 464.306805 | 10021529 |
| 471.308491 | 14195387 |
| 472.311903 | 3772097 |
| 479.229044 | 36842216 |
| 480.228686 | 4345582 |
| 480.232481 | 5499630 |
| 495.266311 | 4329296 |
| 507.224081 | 4512680 |
| 507.329541 | 60418985 |
| 508.333039 | 15190961 |
| 523.255309 | 37497899 |
| 524.254949 | 4126772 |
| 524.258720 | 5945396 |
| 540.426252 | 22604995 |
| 541.429712 | 6319308 |
| 548.467764 | 12201229 |
| 549.471086 | 4188439 |
| 551.355729 | 66235688 |
| 551.357216 | 7486760 |
| 552.359207 | 17014066 |
| 554.551167 | 4035910 |
| 564.462670 | 3083685 |
| 567.281526 | 37752256 |
| 568.281207 | 3873225 |
| 568.284955 | 6469065 |
| 568.457542 | 7538123 |
| 576.499127 | 4044312 |

| m/z | I |
|---|---|
| 594.298421 | 7061186 |
| 595.381953 | 45854413 |
| 595.383640 | 5068493 |
| 596.385468 | 11638486 |
| 605.490320 | 5046059 |
| 611.307803 | 12840800 |
| 639.408328 | 20615240 |
| 640.411664 | 5707855 |
| 655.334080 | 5084338 |
| 683.434482 | 10367277 |
| 684.437849 | 3467568 |
| 685.431654 | 5687602 |
| 685.435548 | 156676402 |
| 685.440720 | 4147506 |
| 686.439151 | 62124340 |
| 687.442746 | 9488694 |
| 699.360352 | 3257668 |
| 727.460826 | 4768008 |




**38d-3**

Chemical Formula: $C_{23}H_{23}BrO$

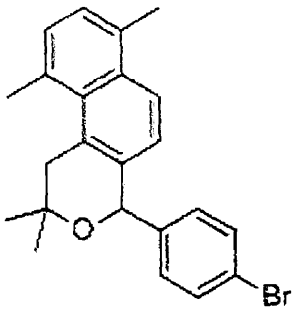
Molecular Weight: 395.34




| | | | | |
|---|---|---|---|---|
| PULSE SEQUENCE<br>Relax. delay 1.000 sec<br>Pulse 14.8 degrees<br>Acq. time 1.998 sec<br>Width 6402.0 Hz<br>8 repetitions | OBSERVE H1, 400.1766985 | DATA PROCESSING<br>FT size 32768<br>Total time 1 minute | | YC-156 pure; 2,5-dimethyl sub. diol with 4-bromo benzaldehyde to form tricyclic isochromene; cdcl3; 5/5/2014<br>Solvent: cdcl3<br>Ambient temperature |

YC-156 pure; 2,5-dimethyl sub. diol with 4-bromo benzaldehyde to form tricyclic isochromene; cdcl3; 5/5/2014

Sample Name:
yc-156

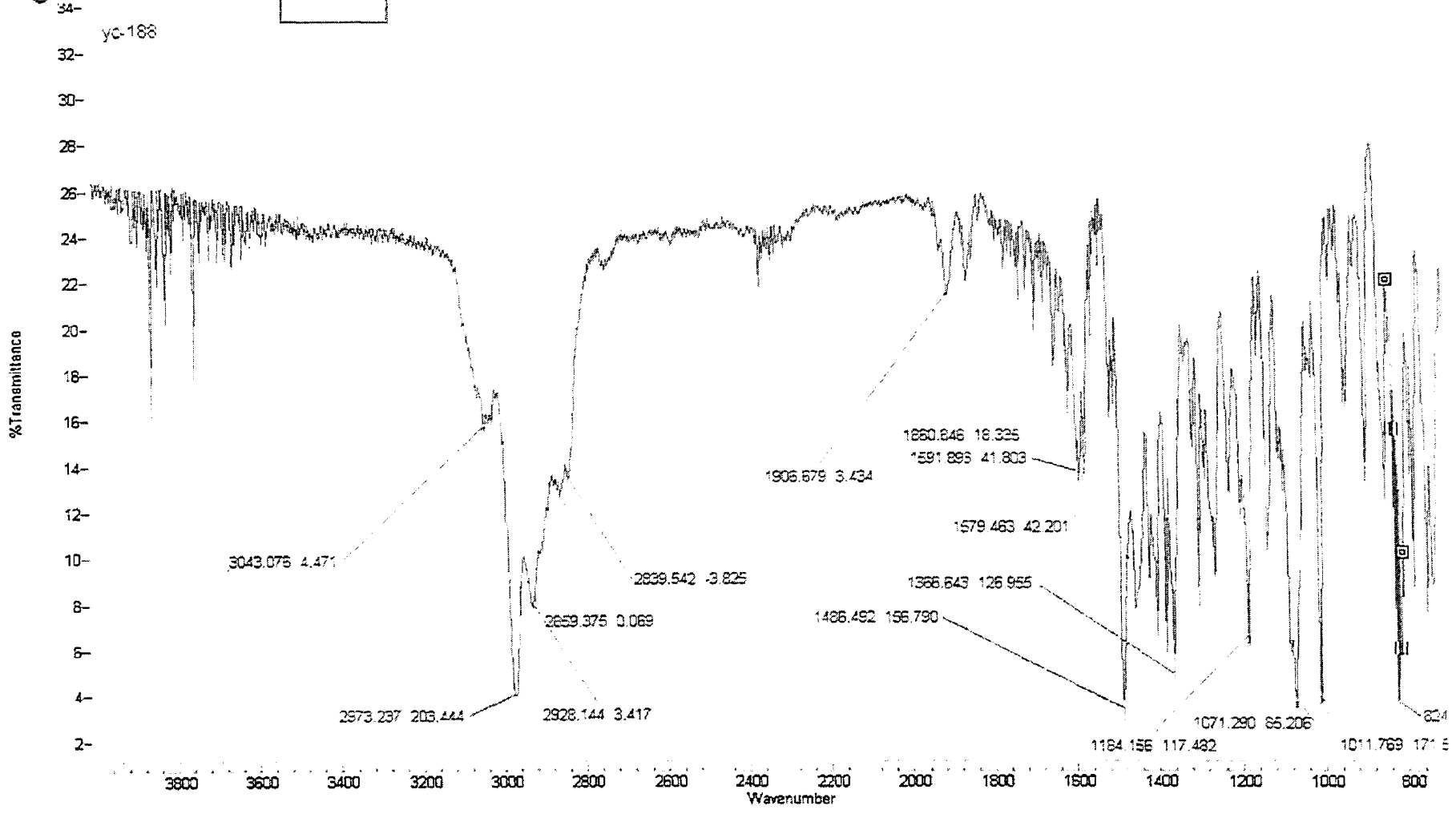



**38d-3**

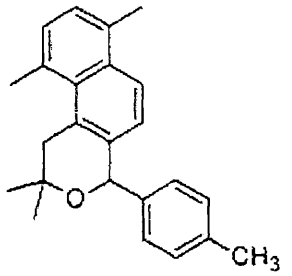
Chemical Formula: $C_{23}H_{23}BrO$

Molecular Weight: 395.34

Digilab Win-IR Pro 38d-3




| | Name | Spectrum |
|---|---|---|
| Spectrum1 | yc-188 | |
| Spectrum2 | | |



**38d-4**

Chemical Formula: $C_{24}H_{26}O$

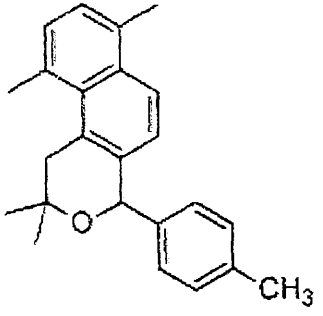
Molecular Weight: 330.47




| | | | | |
|---|---|---|---|---|
| PULSE SEQUENCE<br>Relax. delay 1.000 sec<br>Pulse 45.0 degrees<br>Acq. time 3.408 sec<br>Width 4807.7 Hz<br>4 repetitions | OBSERVE H1, 399.8399051 | DATA PROCESSING<br>FT size 32768<br>Total time 1 minute | | YC-190 pure pdt;<br>2,5-dimethyl-diol with<br>4-methyl-benzaldehyde to<br>form tricyclic<br>isochromene; cdcl3;<br>6/12/2014<br>Solvent: cdcl3<br>Ambient temperature |

YC-190 pure pdt; 2,5-dimethyl-diol with 4-methyl-benzaldehyde to form tricyclic isochromene; cdcl3; 6/12/2014

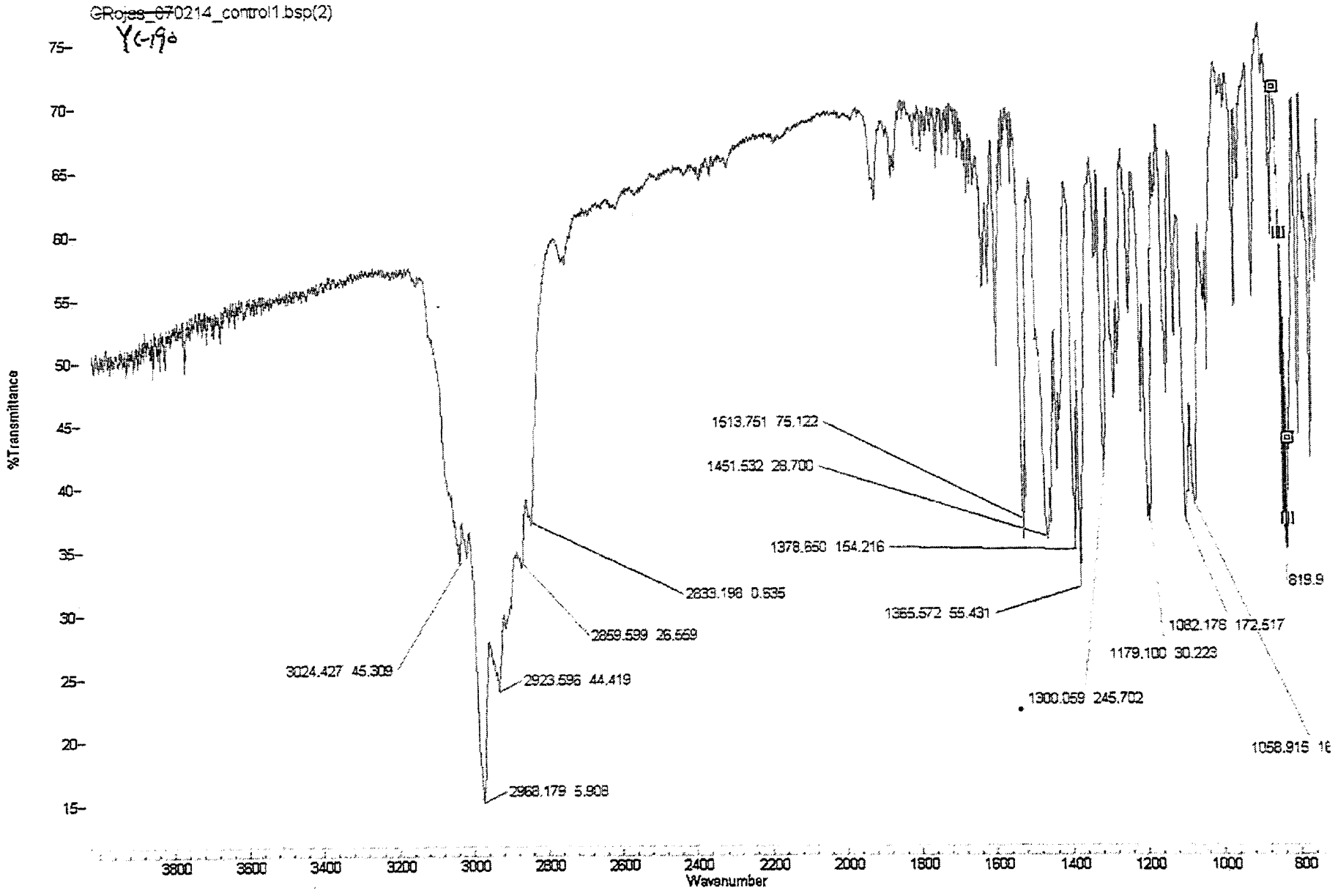
Sample Name:
YC-190-pdt




**38d-4**

Chemical Formula: $C_{24}H_{26}O$
Molecular Weight: 330.47

Digilab Win-IR Pro 38d-4



# Mass Spectrum List Report

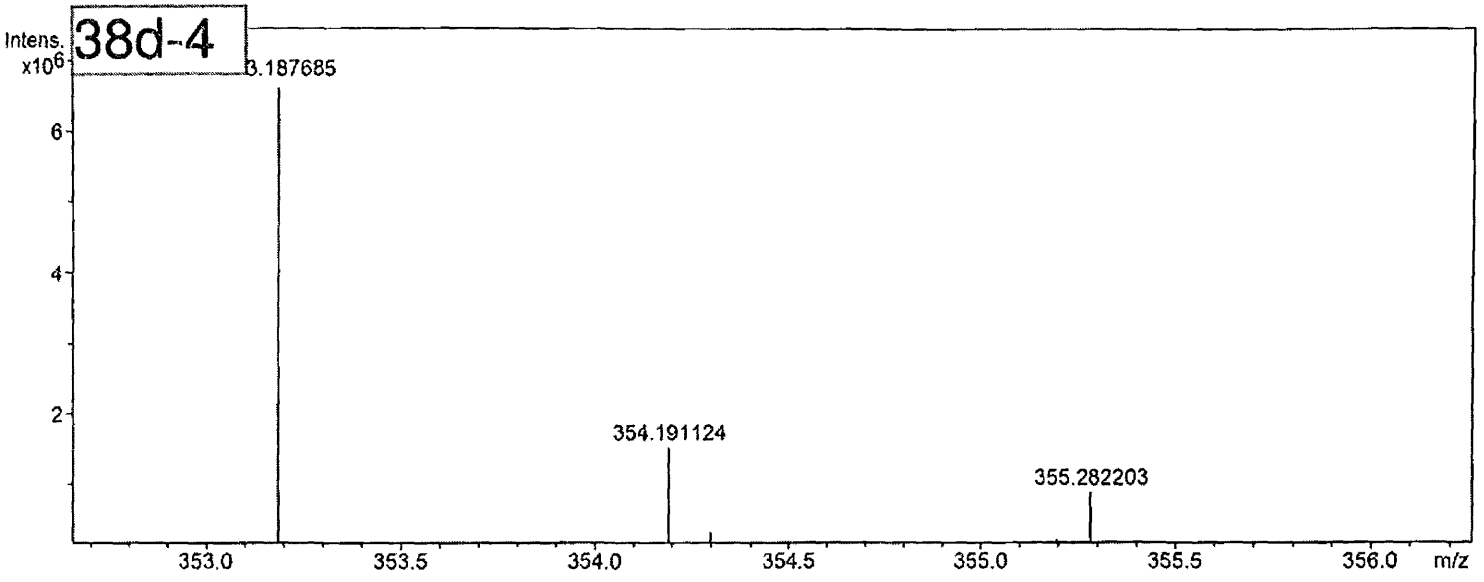


**Analysis Info**

| | | | |
|---|---|---|---|
| Analysis Name | YC-190_pos_000001.d | Acquisition Date | 7/22/2014 4:22:25 PM |
| Method | XMASS_Method | Operator | FTMS_USER |
| Sample Name: | YC-190_pos | Instrument | apex-Qe |
| | YC-190_pos: in 1:1 THF:MeOH w/ NaCl.. | | |

**Acquisition Parameter**

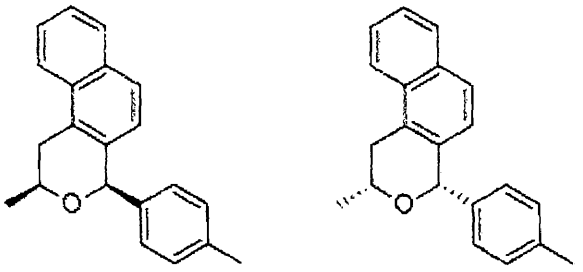
**Sample: YC-190**
**Exact Mass of = (C24H26O)Na+ : 353.187587u**
**Observed Mass = 353.187685u**
**Difference = < 1.0 ppm**




| m/z | I |
|---|---|
| 288.288549 | 17885062 |
| 288.289787 | 185852806 |
| 288.290462 | 7416710 |
| 288.290707 | 4576134 |
| 288.290950 | 3074950 |
| 289.292043 | 7597971 |
| 289.292593 | 3139987 |
| 289.293222 | 60924819 |
| 304.284827 | 31450196 |
| 305.157328 | 3447904 |
| 305.288227 | 4411489 |
| 313.195376 | 2957513 |
| 316.313229 | 3079922 |
| 316.314064 | 2732530 |
| 316.319424 | 15136498 |
| 316.320632 | 52221170 |
| 316.321033 | 260220146 |
| 316.321565 | 21193970 |
| 316.321844 | 11433202 |
| 316.322126 | 7419122 |
| 316.322409 | 4987122 |

| m/z | I |
|---|---|
| 316.322705 | 3582194 |
| 316.322991 | 2773746 |
| 317.322959 | 5770495 |
| 317.323684 | 11474175 |
| 317.324519 | 74294527 |
| 318.328017 | 4436236 |
| 327.078386 | 3027836 |
| 332.315194 | 4252093 |
| 332.316135 | 38798781 |
| 333.319572 | 6752714 |
| 338.303241 | 3304966 |
| 353.187685 | 6690475 |
| 360.347517 | 7229170 |
| 366.278919 | 4837161 |
| 375.250924 | 6890358 |
| 388.543630 | 3157981 |
| 389.214960 | 3072482 |
| 413.266591 | 8501381 |
| 419.277140 | 27027627 |
| 420.280529 | 5533873 |
| 425.287733 | 3152593 |
| 433.241200 | 3437827 |
| 435.202884 | 4768015 |
| 435.344866 | 4478224 |
| 437.192117 | 3449116 |
| 437.193712 | 80177436 |
| 438.197180 | 17246499 |
| 453.167777 | 8262022 |
| 463.302244 | 4188623 |
| 463.303343 | 58730959 |
| 463.304519 | 4610511 |
| 464.306790 | 13277654 |
| 477.267446 | 2988605 |
| 479.229087 | 28486222 |
| 480.228741 | 3373654 |
| 480.232495 | 4478551 |
| 507.224083 | 3396431 |
| 507.329551 | 68823888 |
| 508.333038 | 17783641 |
| 521.345369 | 2772952 |
| 523.255338 | 33303531 |
| 524.254972 | 4112373 |
| 524.258744 | 5866485 |
| 540.426230 | 8244369 |
| 541.429678 | 2806427 |
| 548.467741 | 7263453 |
| 551.355751 | 76442871 |
| 552.359222 | 19426560 |
| 554.551147 | 4143380 |
| 565.371619 | 2826610 |
| 567.281572 | 34295170 |
| 567.329817 | 4027778 |
| 568.281232 | 3910026 |
| 568.284989 | 6749578 |
| 568.457590 | 4629900 |
| 576.499096 | 3190219 |
| 595.381953 | 51818057 |
| 595.383681 | 4535882 |
| 596.385440 | 13704783 |
| 599.553349 | 3255905 |
| 605.490535 | 3665535 |

| m/z | I |
|---|---|
| 611.307814 | 14282393 |
| 611.356121 | 3340953 |
| 612.311241 | 3029661 |
| 639.408372 | 24866542 |
| 640.411756 | 7263984 |
| 655.334093 | 7386886 |
| 683.434602 | 12222224 |
| 684.437972 | 4354832 |
| 685.430827 | 5162768 |
| 685.435615 | 228437776 |
| 685.442092 | 2897680 |
| 686.439174 | 96644880 |
| 686.442976 | 3997456 |
| 687.442860 | 15310607 |
| 699.360356 | 4595466 |
| 701.410110 | 3493641 |
| 727.460810 | 6602488 |
| 771.487033 | 3007239 |



**42a**

Chemical Formula: $C_{21}H_{20}O$

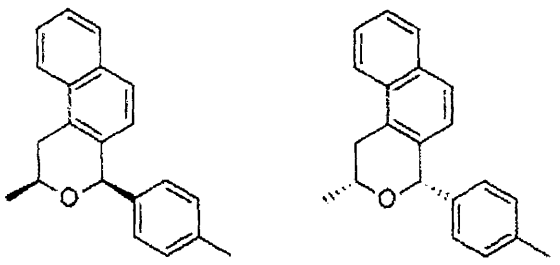
Molecular Weight: 288.39




| | | | | |
|---|---|---|---|---|
| PULSE SEQUENCE<br>Relax. delay 1.000 sec<br>Pulse 45.0 degrees<br>Acq. time 2.556 sec<br>Width 6410.3 Hz<br>8 repetitions | OBSERVE H1, 399.8399131 | DATA PROCESSING<br>FT size 32768<br>Total time 1 minute | | YC-196 cis; (s)-diol with p-tolualdehyde to form tricyclic isochromene; cdcl3; 7/8/2014<br>196<br>Solvent: cdcl3<br>Ambient temperature<br>Operator: rjhink |

YC-194 21-21 pure cis pdt; tricyclic isochromene from racemic diol and p-methyl-benzaldehyde; cdcl3; 6/22/2014

Sample Name:
yc-194-cis

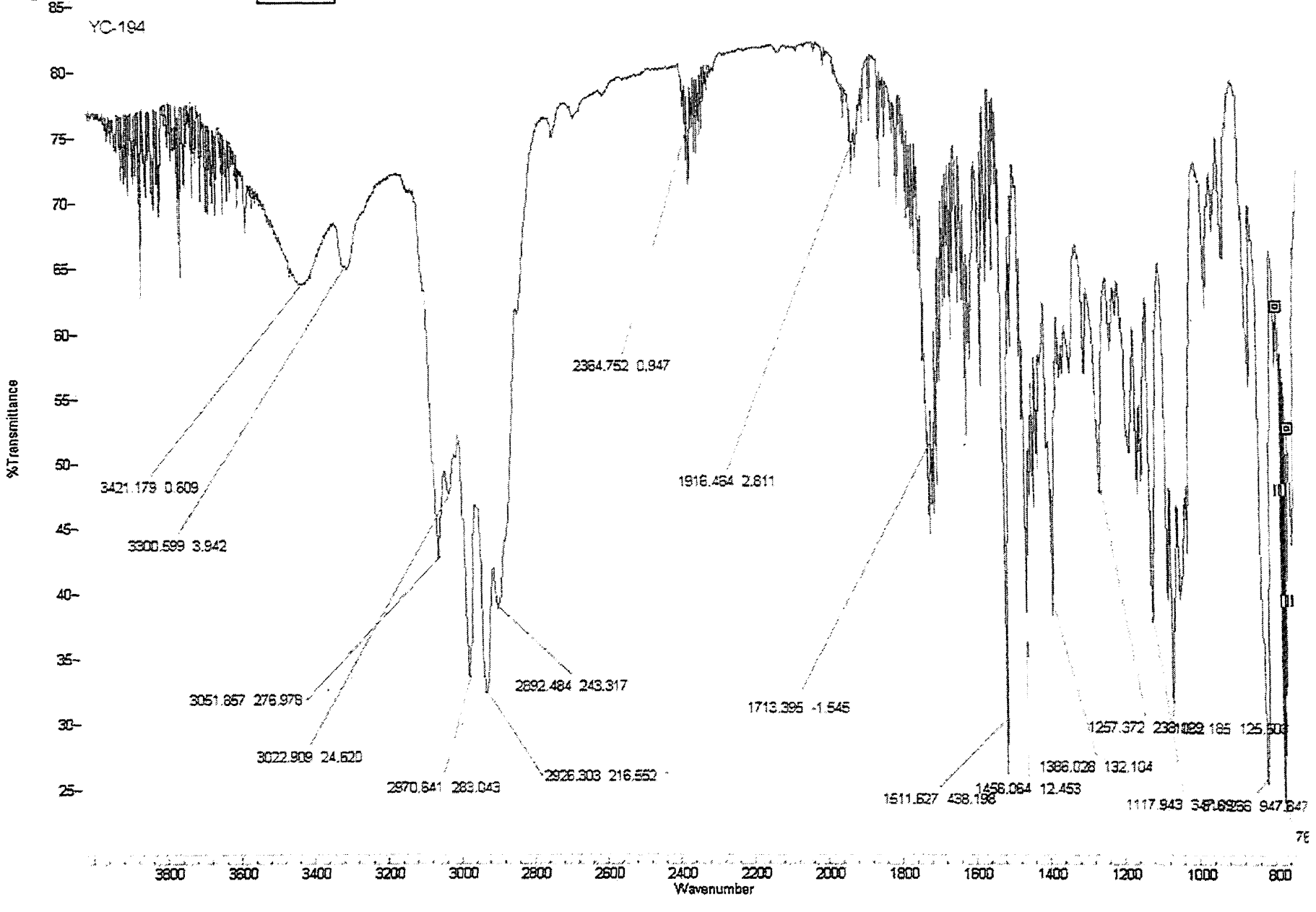


**42a**

Chemical Formula: $C_{21}H_{20}O$

Molecular Weight: 288.39

Digilab Win-IR Pro 42a



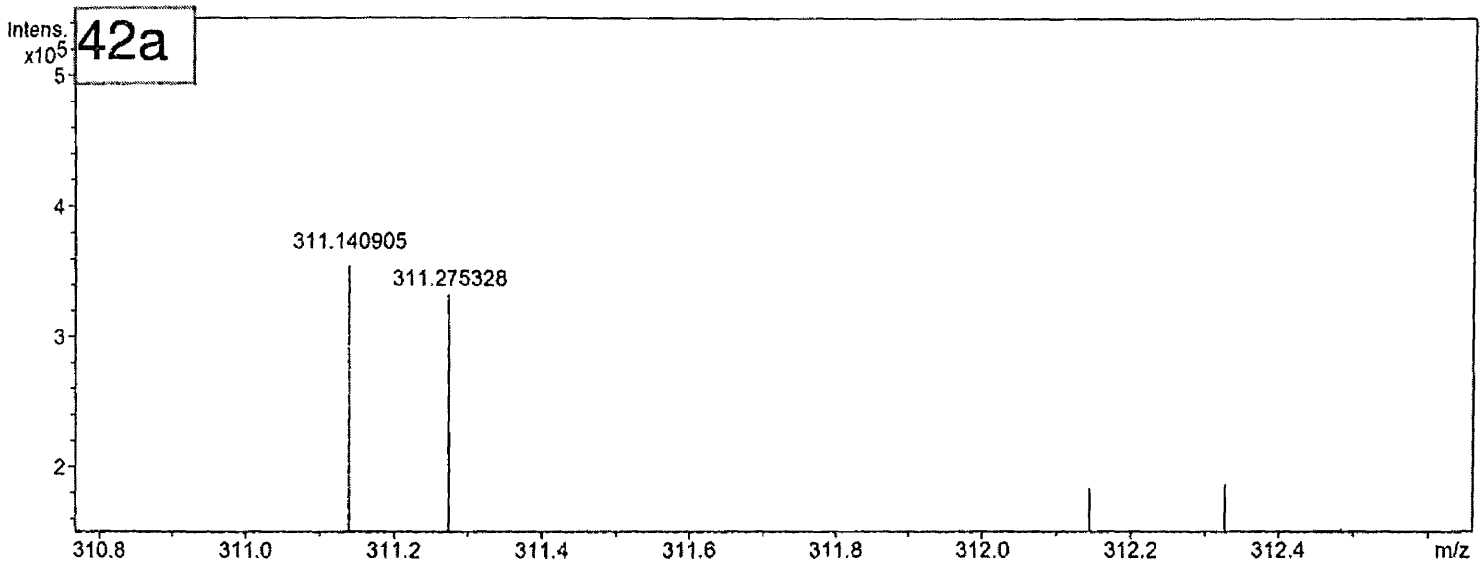
# Mass Spectrum List Report

**Analysis Info**

| | | | |
|---|---|---|---|
| Analysis Name | YC-194_pos_000001.d | Acquisition Date | 7/22/2014 4:37:13 PM |
| Method | XMASS_Method | Operator | FTMS_USER |
| Sample Name: | YC-194_pos | Instrument | apex-Qe |
| | YC-194_pos: in 1:1 THF:MeOH w/ NaCl.. | | |

**Acquisition Parameter**

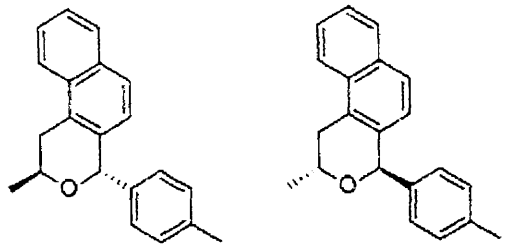
**Sample: YC-194**
**Exact Mass of = (C21H20O)Na+ : 311.140636u**
**Observed Mass = 311.140905u**
**Difference = < 1.0 ppm**




| m/z | I |
|---|---|
| 174.370875 | 4812078 |
| 285.146348 | 10272630 |
| 288.288500 | 17621153 |
| 288.289093 | 12494753 |
| 288.289789 | 203809697 |
| 288.290469 | 8017825 |
| 288.290710 | 4951969 |
| 288.290954 | 3350689 |
| 289.291999 | 6681519 |
| 289.292552 | 4712367 |
| 289.293224 | 61432751 |
| 304.284847 | 27559042 |
| 305.288242 | 4050576 |
| 316.313204 | 3325741 |
| 316.320251 | 43570477 |
| 316.320537 | 48260397 |
| 316.321064 | 272770349 |
| 316.321841 | 12367149 |
| 316.322123 | 7843117 |
| 316.322405 | 5093677 |
| 316.322706 | 3723053 |

| m/z | I |
|---|---|
| 317.323403 | 9204027 |
| 317.324518 | 86451515 |
| 318.328030 | 4482889 |
| 325.120184 | 17384871 |
| 326.123545 | 3546549 |
| 332.315175 | 3412488 |
| 332.316142 | 42419720 |
| 333.319591 | 7385621 |
| 338.303258 | 4541525 |
| 343.130774 | 3281040 |
| 343.188286 | 10794641 |
| 357.203939 | 12881707 |
| 360.347532 | 7464778 |
| 366.278947 | 5308289 |
| 373.198892 | 3881916 |
| 375.250936 | 6535117 |
| 388.543460 | 3668527 |
| 389.214965 | 3424820 |
| 413.266603 | 14911685 |
| 414.269987 | 3380938 |
| 419.277149 | 28870885 |
| 420.280528 | 5621994 |
| 425.287761 | 4523268 |
| 433.241208 | 4035885 |
| 435.202907 | 5019959 |
| 435.344896 | 5273912 |
| 437.192127 | 3608897 |
| 437.192768 | 7043393 |
| 437.193714 | 89745729 |
| 438.197192 | 18999622 |
| 441.297945 | 11213142 |
| 453.167814 | 8018325 |
| 463.302203 | 3922382 |
| 463.303366 | 55503310 |
| 463.304537 | 4358606 |
| 464.306816 | 12005844 |
| 477.267463 | 3974694 |
| 479.229093 | 32016947 |
| 480.228732 | 4005434 |
| 480.232503 | 5281338 |
| 507.224089 | 3676935 |
| 507.328244 | 5188360 |
| 507.329568 | 69856008 |
| 507.330971 | 4942600 |
| 508.333061 | 17500944 |
| 521.293695 | 3263356 |
| 523.255339 | 40094605 |
| 524.254984 | 4786070 |
| 524.258765 | 6632342 |
| 540.426326 | 8053795 |
| 548.467807 | 7353450 |
| 550.628997 | 3433597 |
| 551.355789 | 70331523 |
| 552.359239 | 18594956 |
| 554.551191 | 4493471 |
| 567.281575 | 39431439 |
| 567.329849 | 3352847 |
| 568.281199 | 4772119 |
| 568.285016 | 7470359 |
| 568.457593 | 3975449 |
| 595.382009 | 45444599 |

| m/z | I |
|---|---|
| 596.385486 | 11996671 |
| 605.490485 | 4041284 |
| 611.307849 | 17018479 |
| 612.311211 | 3830390 |
| 639.408410 | 23007013 |
| 640.411795 | 6731563 |
| 655.334102 | 9066363 |
| 683.434639 | 11460595 |
| 684.438019 | 4212727 |
| 685.430762 | 4816890 |
| 685.432142 | 7002106 |
| 685.435642 | 214478842 |
| 686.439216 | 88256510 |
| 686.442963 | 3583998 |
| 687.442911 | 13889537 |
| 699.360381 | 5693476 |
| 701.410134 | 3796009 |
| 727.460856 | 5408852 |



**42b**

Chemical Formula: $C_{21}H_{20}O$

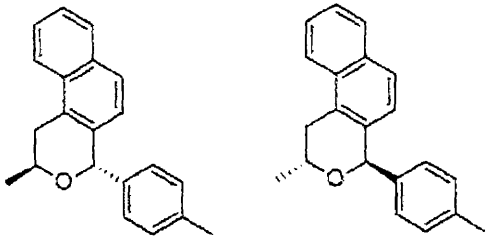
Molecular Weight: 288.39




| | | | | |
|---|---|---|---|---|
| PULSE SEQUENCE<br>Relax. delay 1.000 sec<br>Pulse 45.0 degrees<br>Acq. time 2.556 sec<br>Width 6410.3 Hz<br>8 repetitions | OBSERVE H1, 399.8398951 | DATA PROCESSING<br>FT size 32768<br>Total time 1 minute | | YC-196 trans; (s)-diol with p-tolualdehyde to form tricyclic isochromene; cdcl3; 7/8/2014<br>205<br>Solvent: cdcl3<br>Ambient temperature |

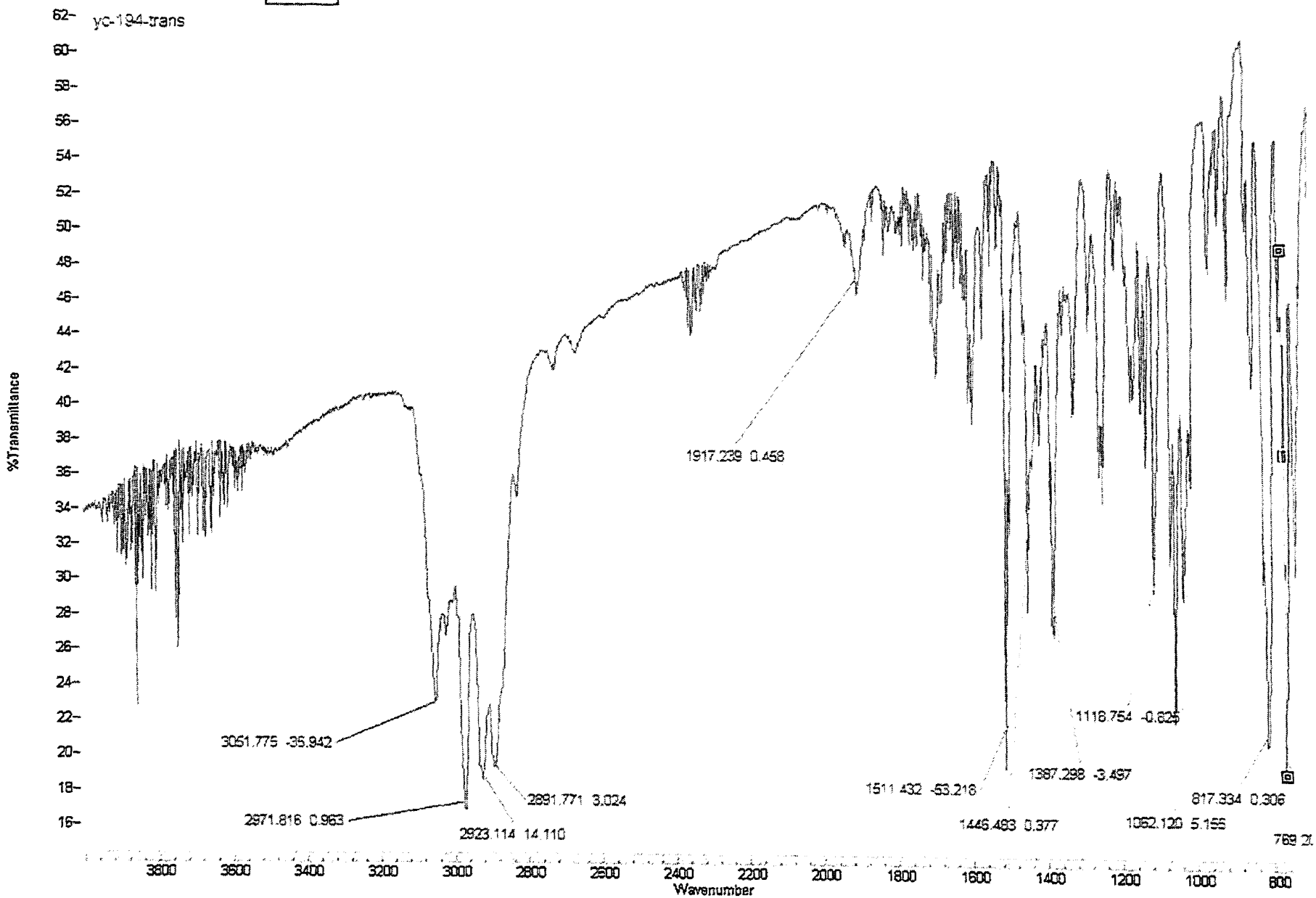
YC-194 trans compd; racemic diol with p-methyl-benzaldehyde to form tricyclic isochromene; cdcl3; 6/26/2014

Sample Name:
yc-194-trans



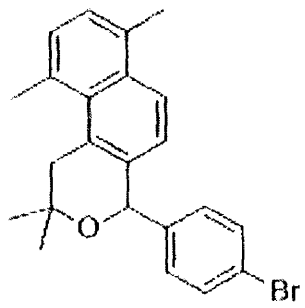
**42b**
Chemical Formula: $C_{21}H_{20}O$
Molecular Weight: 288.39

Digilab Win-IR Pro 42b



Crystallographic Data for:

**4-(4-bromophenyl)-2,2,7,10-tetramethyl-1,4-dihydro-2H-benzo[f]iso-chromene (38d-3):**




**38d-3**
Chemical Formula: $C_{23}H_{23}BrO$
Molecular Weight: 395.34

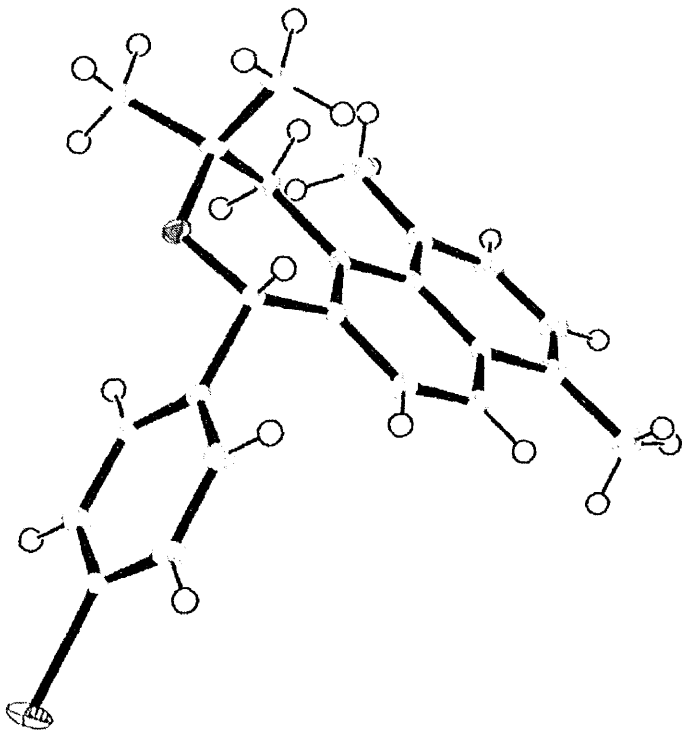


**Table 1. Crystal data and structure refinement for P21onn.res.**

| | | |
|---|---|---|
| Identification code | P21onn | |
| Empirical formula | C23 H23 Br O | |
| Formula weight | 395.32 | |
| Temperature | 100(2) K | |
| Wavelength | 1.54178 Å | |
| Crystal system | Monoclinic | |
| Space group | P 21/n | |
| Unit cell dimensions | a = 17.0425(3) Å | α= 90°. |
| | b = 6.45510(10) Å | β= 95.9170(6)°. |
| | c = 17.1404(3) Å | γ = 90°. |
| Volume | 1875.59(5) $Å^3$ | |
| Z | 4 | |
| Density (calculated) | 1.400 $Mg/m^3$ | |
| Absorption coefficient | 3.026 $mm^{-1}$ | |
| F(000) | 816 | |
| Crystal size | 0.555 x 0.248 x 0.189 $mm^3$ | |
| Theta range for data collection | 3.482 to 66.992°. | |
| Index ranges | -20<=h<=20, -7<=k<=6, -20<=l<=19 | |
| Reflections collected | 20549 | |
| Independent reflections | 3309 [R(int) = 0.0304] | |
| Completeness to theta = 67.679° | 97.5 % | |
| Refinement method | Full-matrix least-squares on $F^2$ | |
| Data / restraints / parameters | 3309 / 0 / 230 | |
| Goodness-of-fit on $F^2$ | 1.031 | |
| Final R indices [I>2sigma(I)] | R1 = 0.0242, wR2 = 0.0654 | |
| R indices (all data) | R1 = 0.0245, wR2 = 0.0656 | |
| Extinction coefficient | n/a | |
| Largest diff. peak and hole | 0.411 and -0.380 $e.Å^{-3}$ | |

**Table 2. Atomic coordinates ( x $10^4$) and equivalent isotropic displacement parameters ($Å^2$x $10^3$).**

for P21onn.res. U(eq) is defined as one third of the trace of the orthogonalized $U^{ij}$ tensor.

| | x | y | z | U(eq) |
|---|---|---|---|---|
| Br(1) | 323(1) | -321(1) | 1174(1) | 24(1) |
| O(1) | 2838(1) | -208(2) | 4459(1) | 16(1) |
| C(1) | 2504(1) | 236(2) | 5790(1) | 15(1) |
| C(2) | 3160(1) | -224(2) | 5272(1) | 16(1) |
| C(3) | 2512(1) | 1713(2) | 4184(1) | 14(1) |
| C(4) | 2029(1) | 2786(2) | 4767(1) | 13(1) |
| C(5) | 1608(1) | 4566(2) | 4486(1) | 16(1) |
| C(6) | 1170(1) | 5654(2) | 4960(1) | 16(1) |
| C(7) | 1110(1) | 5028(2) | 5746(1) | 14(1) |
| C(8) | 637(1) | 6244(3) | 6212(1) | 18(1) |
| C(9) | 554(1) | 5601(3) | 6960(1) | 21(1) |
| C(10) | 930(1) | 3788(3) | 7255(1) | 20(1) |
| C(11) | 1408(1) | 2581(3) | 6838(1) | 17(1) |
| C(12) | 1523(1) | 3204(2) | 6046(1) | 14(1) |
| C(13) | 2007(1) | 2119(2) | 5530(1) | 13(1) |
| C(14) | 3446(1) | -2443(3) | 5403(1) | 22(1) |
| C(15) | 3840(1) | 1308(3) | 5415(1) | 22(1) |
| C(16) | 2003(1) | 1217(2) | 3426(1) | 12(1) |
| C(17) | 2002(1) | 2459(2) | 2762(1) | 16(1) |
| C(18) | 1507(1) | 2019(3) | 2085(1) | 17(1) |
| C(19) | 1022(1) | 299(3) | 2080(1) | 16(1) |
| C(20) | 1024(1) | -995(3) | 2727(1) | 16(1) |
| C(21) | 1516(1) | -517(2) | 3397(1) | 15(1) |
| C(22) | 232(1) | 8199(3) | 5892(1) | 23(1) |
| C(23) | 1753(1) | 679(3) | 7264(1) | 23(1) |

**Table 3. Bond lengths [Å] and angles [°] for P21onn.res.**

| | |
|---|---|
| Br(1)-C(19) | 1.8991(17) |
| O(1)-C(3) | 1.4198(18) |
| O(1)-C(2) | 1.443(2) |
| C(1)-C(13) | 1.522(2) |
| C(1)-C(2) | 1.526(2) |
| C(1)-H(1A) | 0.9900 |
| C(1)-H(1B) | 0.9900 |
| C(2)-C(14) | 1.522(2) |
| C(2)-C(15) | 1.525(2) |
| C(3)-C(16) | 1.520(2) |
| C(3)-C(4) | 1.526(2) |
| C(3)-H(3) | 1.0000 |
| C(4)-C(13) | 1.381(2) |
| C(4)-C(5) | 1.412(2) |
| C(5)-C(6) | 1.356(2) |
| C(5)-H(5) | 0.9500 |
| C(6)-C(7) | 1.420(2) |
| C(6)-H(6) | 0.9500 |
| C(7)-C(8) | 1.427(2) |
| C(7)-C(12) | 1.439(2) |
| C(8)-C(9) | 1.369(2) |
| C(8)-C(22) | 1.514(2) |
| C(9)-C(10) | 1.403(3) |
| C(9)-H(9) | 0.9500 |
| C(10)-C(11) | 1.378(2) |
| C(10)-H(10) | 0.9500 |
| C(11)-C(12) | 1.448(2) |
| C(11)-C(23) | 1.516(2) |
| C(12)-C(13) | 1.451(2) |
| C(14)-H(14A) | 0.9800 |
| C(14)-H(14B) | 0.9800 |
| C(14)-H(14C) | 0.9800 |
| C(15)-H(15A) | 0.9800 |

| | |
|---|---|
| C(15)-H(15B) | 0.9800 |
| C(15)-H(15C) | 0.9800 |
| C(16)-C(17) | 1.391(2) |
| C(16)-C(21) | 1.392(2) |
| C(17)-C(18) | 1.392(2) |
| C(17)-H(17) | 0.9500 |
| C(18)-C(19) | 1.384(2) |
| C(18)-H(18) | 0.9500 |
| C(19)-C(20) | 1.388(2) |
| C(20)-C(21) | 1.385(2) |
| C(20)-H(20) | 0.9500 |
| C(21)-H(21) | 0.9500 |
| C(22)-H(22A) | 0.9800 |
| C(22)-H(22B) | 0.9800 |
| C(22)-H(22C) | 0.9800 |
| C(23)-H(23A) | 0.9800 |
| C(23)-H(23B) | 0.9800 |
| C(23)-H(23C) | 0.9800 |

| | |
|---|---|
| C(3)-O(1)-C(2) | 115.05(11) |
| C(13)-C(1)-C(2) | 113.79(13) |
| C(13)-C(1)-H(1A) | 108.8 |
| C(2)-C(1)-H(1A) | 108.8 |
| C(13)-C(1)-H(1B) | 108.8 |
| C(2)-C(1)-H(1B) | 108.8 |
| H(1A)-C(1)-H(1B) | 107.7 |
| O(1)-C(2)-C(14) | 103.48(13) |
| O(1)-C(2)-C(15) | 110.94(14) |
| C(14)-C(2)-C(15) | 111.05(14) |
| O(1)-C(2)-C(1) | 109.46(13) |
| C(14)-C(2)-C(1) | 109.88(14) |
| C(15)-C(2)-C(1) | 111.73(13) |
| O(1)-C(3)-C(16) | 105.64(12) |
| O(1)-C(3)-C(4) | 113.46(12) |
| C(16)-C(3)-C(4) | 110.89(12) |
| O(1)-C(3)-H(3) | 108.9 |

| | |
|---|---|
| C(16)-C(3)-H(3) | 108.9 |
| C(4)-C(3)-H(3) | 108.9 |
| C(13)-C(4)-C(5) | 120.93(14) |
| C(13)-C(4)-C(3) | 123.24(14) |
| C(5)-C(4)-C(3) | 115.81(13) |
| C(6)-C(5)-C(4) | 120.63(15) |
| C(6)-C(5)-H(5) | 119.7 |
| C(4)-C(5)-H(5) | 119.7 |
| C(5)-C(6)-C(7) | 121.23(15) |
| C(5)-C(6)-H(6) | 119.4 |
| C(7)-C(6)-H(6) | 119.4 |
| C(6)-C(7)-C(8) | 118.27(15) |
| C(6)-C(7)-C(12) | 119.47(14) |
| C(8)-C(7)-C(12) | 122.26(15) |
| C(9)-C(8)-C(7) | 118.41(15) |
| C(9)-C(8)-C(22) | 120.36(15) |
| C(7)-C(8)-C(22) | 121.23(15) |
| C(8)-C(9)-C(10) | 120.19(15) |
| C(8)-C(9)-H(9) | 119.9 |
| C(10)-C(9)-H(9) | 119.9 |
| C(11)-C(10)-C(9) | 123.86(15) |
| C(11)-C(10)-H(10) | 118.1 |
| C(9)-C(10)-H(10) | 118.1 |
| C(10)-C(11)-C(12) | 118.24(15) |
| C(10)-C(11)-C(23) | 115.35(14) |
| C(12)-C(11)-C(23) | 126.40(15) |
| C(7)-C(12)-C(11) | 116.97(14) |
| C(7)-C(12)-C(13) | 117.69(14) |
| C(11)-C(12)-C(13) | 125.33(14) |
| C(4)-C(13)-C(12) | 119.99(14) |
| C(4)-C(13)-C(1) | 117.25(14) |
| C(12)-C(13)-C(1) | 122.75(13) |
| C(2)-C(14)-H(14A) | 109.5 |
| C(2)-C(14)-H(14B) | 109.5 |
| H(14A)-C(14)-H(14B) | 109.5 |
| C(2)-C(14)-H(14C) | 109.5 |

| | |
|---|---|
| H(14A)-C(14)-H(14C) | 109.5 |
| H(14B)-C(14)-H(14C) | 109.5 |
| C(2)-C(15)-H(15A) | 109.5 |
| C(2)-C(15)-H(15B) | 109.5 |
| H(15A)-C(15)-H(15B) | 109.5 |
| C(2)-C(15)-H(15C) | 109.5 |
| H(15A)-C(15)-H(15C) | 109.5 |
| H(15B)-C(15)-H(15C) | 109.5 |
| C(17)-C(16)-C(21) | 118.92(14) |
| C(17)-C(16)-C(3) | 122.06(14) |
| C(21)-C(16)-C(3) | 119.02(14) |
| C(16)-C(17)-C(18) | 120.99(15) |
| C(16)-C(17)-H(17) | 119.5 |
| C(18)-C(17)-H(17) | 119.5 |
| C(19)-C(18)-C(17) | 118.59(15) |
| C(19)-C(18)-H(18) | 120.7 |
| C(17)-C(18)-H(18) | 120.7 |
| C(18)-C(19)-C(20) | 121.69(15) |
| C(18)-C(19)-Br(1) | 119.84(12) |
| C(20)-C(19)-Br(1) | 118.47(12) |
| C(21)-C(20)-C(19) | 118.71(15) |
| C(21)-C(20)-H(20) | 120.6 |
| C(19)-C(20)-H(20) | 120.6 |
| C(20)-C(21)-C(16) | 121.07(15) |
| C(20)-C(21)-H(21) | 119.5 |
| C(16)-C(21)-H(21) | 119.5 |
| C(8)-C(22)-H(22A) | 109.5 |
| C(8)-C(22)-H(22B) | 109.5 |
| H(22A)-C(22)-H(22B) | 109.5 |
| C(8)-C(22)-H(22C) | 109.5 |
| H(22A)-C(22)-H(22C) | 109.5 |
| H(22B)-C(22)-H(22C) | 109.5 |
| C(11)-C(23)-H(23A) | 109.5 |
| C(11)-C(23)-H(23B) | 109.5 |
| H(23A)-C(23)-H(23B) | 109.5 |
| C(11)-C(23)-H(23C) | 109.5 |

| | |
|---|---|
| H(23A)-C(23)-H(23C) | 109.5 |
| H(23B)-C(23)-H(23C) | 109.5 |

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Symmetry transformations used to generate equivalent atoms:

**Table 4. Anisotropic displacement parameters ($Å^2 x\ 10^3$) for P21onn.res. The anisotropic displacement factor exponent takes the form: $-2\pi^2[\ h^2\ a^{*2}U^{11} + ... + 2\ h\ k\ a^*\ b^*\ U^{12}\ ]$.**

| | $U^{11}$ | $U^{22}$ | $U^{33}$ | $U^{23}$ | $U^{13}$ | $U^{12}$ |
|---|---|---|---|---|---|---|
| Br(1) | 17(1) | 38(1) | 16(1) | -1(1) | -6(1) | -4(1) |
| O(1) | 20(1) | 17(1) | 12(1) | -1(1) | -4(1) | 7(1) |
| C(1) | 17(1) | 14(1) | 13(1) | 1(1) | -2(1) | 0(1) |
| C(2) | 15(1) | 19(1) | 12(1) | 0(1) | -5(1) | 3(1) |
| C(3) | 14(1) | 14(1) | 13(1) | 1(1) | 0(1) | 1(1) |
| C(4) | 12(1) | 12(1) | 14(1) | -2(1) | -1(1) | -2(1) |
| C(5) | 21(1) | 14(1) | 13(1) | 2(1) | 2(1) | -1(1) |
| C(6) | 17(1) | 11(1) | 19(1) | 2(1) | 1(1) | 1(1) |
| C(7) | 13(1) | 13(1) | 16(1) | -2(1) | 0(1) | -4(1) |
| C(8) | 14(1) | 17(1) | 23(1) | -3(1) | 2(1) | -2(1) |
| C(9) | 18(1) | 26(1) | 21(1) | -6(1) | 6(1) | -1(1) |
| C(10) | 22(1) | 26(1) | 13(1) | -2(1) | 3(1) | -5(1) |
| C(11) | 18(1) | 18(1) | 14(1) | -1(1) | -1(1) | -5(1) |
| C(12) | 14(1) | 13(1) | 14(1) | -2(1) | -1(1) | -5(1) |
| C(13) | 13(1) | 12(1) | 14(1) | -1(1) | -2(1) | -3(1) |
| C(14) | 24(1) | 22(1) | 17(1) | -1(1) | -5(1) | 9(1) |
| C(15) | 16(1) | 28(1) | 23(1) | 1(1) | -2(1) | -1(1) |
| C(16) | 10(1) | 15(1) | 13(1) | -2(1) | 2(1) | 3(1) |
| C(17) | 15(1) | 16(1) | 17(1) | 1(1) | 2(1) | -2(1) |
| C(18) | 18(1) | 20(1) | 14(1) | 5(1) | 1(1) | 2(1) |
| C(19) | 10(1) | 23(1) | 13(1) | -2(1) | -1(1) | 3(1) |
| C(20) | 14(1) | 17(1) | 18(1) | -2(1) | 3(1) | -2(1) |
| C(21) | 16(1) | 15(1) | 14(1) | 2(1) | 3(1) | 1(1) |
| C(22) | 21(1) | 20(1) | 28(1) | -2(1) | 5(1) | 4(1) |
| C(23) | 32(1) | 25(1) | 14(1) | 4(1) | 5(1) | 2(1) |

**Table 5. Hydrogen coordinates ( x $10^4$) and isotropic displacement parameters ($Å^2$x $10^3$) for P21onn.res.**

| | x | y | z | U(eq) |
|---|---|---|---|---|
| H(1A) | 2155 | -989 | 5792 | 18 |
| H(1B) | 2743 | 460 | 6335 | 18 |
| H(3) | 2950 | 2654 | 4064 | 16 |
| H(5) | 1633 | 5004 | 3960 | 19 |
| H(6) | 897 | 6858 | 4763 | 19 |
| H(9) | 241 | 6384 | 7281 | 25 |
| H(10) | 850 | 3367 | 7772 | 24 |
| H(14A) | 3628 | -2644 | 5959 | 32 |
| H(14B) | 3882 | -2709 | 5086 | 32 |
| H(14C) | 3012 | -3402 | 5248 | 32 |
| H(15A) | 4097 | 1129 | 5949 | 34 |
| H(15B) | 3638 | 2725 | 5351 | 34 |
| H(15C) | 4224 | 1054 | 5037 | 34 |
| H(17) | 2343 | 3624 | 2772 | 19 |
| H(18) | 1503 | 2880 | 1635 | 21 |
| H(20) | 696 | -2186 | 2711 | 20 |
| H(21) | 1521 | -1387 | 3845 | 18 |
| H(22A) | 626 | 9150 | 5715 | 35 |
| H(22B) | -36 | 8865 | 6304 | 35 |
| H(22C) | -155 | 7848 | 5449 | 35 |
| H(23A) | 1488 | 450 | 7738 | 35 |
| H(23B) | 2318 | 889 | 7410 | 35 |
| H(23C) | 1675 | -531 | 6920 | 35 |

**Table 6. Torsion angles [°] for P21onn.res.**

| | |
|---|---|
| C(3)-O(1)-C(2)-C(14) | 178.98(13) |
| C(3)-O(1)-C(2)-C(15) | -61.87(17) |
| C(3)-O(1)-C(2)-C(1) | 61.89(17) |
| C(13)-C(1)-C(2)-O(1) | -48.91(17) |
| C(13)-C(1)-C(2)-C(14) | -161.91(13) |
| C(13)-C(1)-C(2)-C(15) | 74.37(17) |
| C(2)-O(1)-C(3)-C(16) | -163.29(12) |
| C(2)-O(1)-C(3)-C(4) | -41.61(17) |
| O(1)-C(3)-C(4)-C(13) | 9.2(2) |
| C(16)-C(3)-C(4)-C(13) | 127.87(15) |
| O(1)-C(3)-C(4)-C(5) | -172.20(13) |
| C(16)-C(3)-C(4)-C(5) | -53.49(18) |
| C(13)-C(4)-C(5)-C(6) | -0.4(2) |
| C(3)-C(4)-C(5)-C(6) | -179.02(14) |
| C(4)-C(5)-C(6)-C(7) | -0.9(2) |
| C(5)-C(6)-C(7)-C(8) | -179.91(15) |
| C(5)-C(6)-C(7)-C(12) | 0.0(2) |
| C(6)-C(7)-C(8)-C(9) | 177.55(15) |
| C(12)-C(7)-C(8)-C(9) | -2.4(2) |
| C(6)-C(7)-C(8)-C(22) | -2.3(2) |
| C(12)-C(7)-C(8)-C(22) | 177.76(15) |
| C(7)-C(8)-C(9)-C(10) | 0.1(2) |
| C(22)-C(8)-C(9)-C(10) | 179.99(16) |
| C(8)-C(9)-C(10)-C(11) | 1.5(3) |
| C(9)-C(10)-C(11)-C(12) | -0.7(2) |
| C(9)-C(10)-C(11)-C(23) | -179.69(16) |
| C(6)-C(7)-C(12)-C(11) | -176.91(14) |
| C(8)-C(7)-C(12)-C(11) | 3.0(2) |
| C(6)-C(7)-C(12)-C(13) | 2.0(2) |
| C(8)-C(7)-C(12)-C(13) | -178.11(14) |
| C(10)-C(11)-C(12)-C(7) | -1.4(2) |
| C(23)-C(11)-C(12)-C(7) | 177.39(15) |
| C(10)-C(11)-C(12)-C(13) | 179.78(15) |

| | |
|---|---|
| C(23)-C(11)-C(12)-C(13) | -1.4(3) |
| C(5)-C(4)-C(13)-C(12) | 2.4(2) |
| C(3)-C(4)-C(13)-C(12) | -179.02(13) |
| C(5)-C(4)-C(13)-C(1) | -177.68(14) |
| C(3)-C(4)-C(13)-C(1) | 0.9(2) |
| C(7)-C(12)-C(13)-C(4) | -3.2(2) |
| C(11)-C(12)-C(13)-C(4) | 175.62(14) |
| C(7)-C(12)-C(13)-C(1) | 176.93(14) |
| C(11)-C(12)-C(13)-C(1) | -4.3(2) |
| C(2)-C(1)-C(13)-C(4) | 19.2(2) |
| C(2)-C(1)-C(13)-C(12) | -160.89(14) |
| O(1)-C(3)-C(16)-C(17) | -137.29(14) |
| C(4)-C(3)-C(16)-C(17) | 99.38(16) |
| O(1)-C(3)-C(16)-C(21) | 43.57(17) |
| C(4)-C(3)-C(16)-C(21) | -79.75(17) |
| C(21)-C(16)-C(17)-C(18) | 1.7(2) |
| C(3)-C(16)-C(17)-C(18) | -177.43(14) |
| C(16)-C(17)-C(18)-C(19) | -0.8(2) |
| C(17)-C(18)-C(19)-C(20) | -0.8(2) |
| C(17)-C(18)-C(19)-Br(1) | 178.74(12) |
| C(18)-C(19)-C(20)-C(21) | 1.4(2) |
| Br(1)-C(19)-C(20)-C(21) | -178.17(12) |
| C(19)-C(20)-C(21)-C(16) | -0.4(2) |
| C(17)-C(16)-C(21)-C(20) | -1.1(2) |
| C(3)-C(16)-C(21)-C(20) | 178.04(14) |

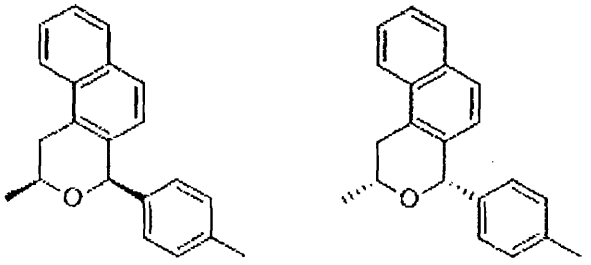
Symmetry transformations used to generate equivalent atoms:

**Table 7. Hydrogen bonds for P21onn.res [Å and °].**

| D-H...A | d(D-H) | d(H...A) | d(D...A) | <(DHA) |
|---|---|---|---|---|

Crystallographic Data for:

**(2S,4R)-2-methyl-4-(p-tolyl)-1,4-dihydro-2H-benzo[f]isochromene (42a)**



**42a**

Chemical Formula: $C_{21}H_{20}O$

Molecular Weight: 288.39

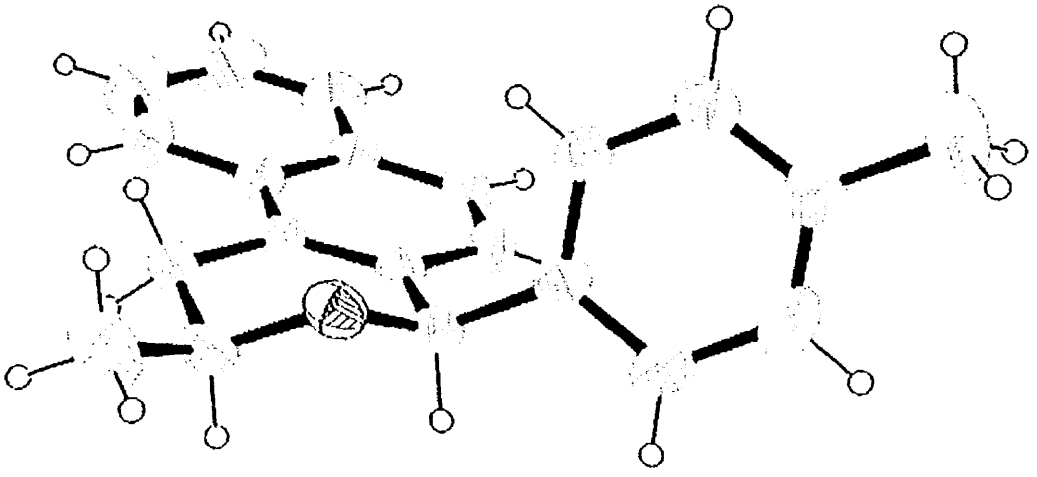


**Table 8.** Crystal data and structure refinement for Pbca.res.

| | | |
|---|---|---|
| Identification code | Pbca | |
| Empirical formula | C21 H20 O | |
| Formula weight | 288.37 | |
| Temperature | 296(2) K | |
| Wavelength | 1.54178 Å | |
| Crystal system | Orthorhombic | |
| Space group | P b c a | |
| Unit cell dimensions | a = 18.1842(2) Å | α= 90°. |
| | b = 8.95420(10) Å | β= 90°. |
| | c = 20.2236(2) Å | γ = 90°. |
| Volume | 3292.91(6) $Å^3$ | |
| Z | 8 | |
| Density (calculated) | 1.163 $Mg/m^3$ | |
| Absorption coefficient | 0.536 $mm^{-1}$ | |
| F(000) | 1232 | |
| Crystal size | 0.450 x 0.170 x 0.100 $mm^3$ | |
| Theta range for data collection | 4.864 to 64.984°. | |
| Index ranges | -21<=h<=21, -10<=k<=10, -20<=l<=23 | |
| Reflections collected | 22603 | |
| Independent reflections | 2790 [R(int) = 0.0350] | |
| Completeness to theta = 67.679° | 93.5 % | |
| Refinement method | Full-matrix least-squares on $F^2$ | |
| Data / restraints / parameters | 2790 / 0 / 201 | |
| Goodness-of-fit on $F^2$ | 1.026 | |
| Final R indices [I>2sigma(I)] | R1 = 0.0406, wR2 = 0.1157 | |
| R indices (all data) | R1 = 0.0488, wR2 = 0.1246 | |
| Extinction coefficient | 0.00126(18) | |
| Largest diff. peak and hole | 0.144 and -0.121 $e.Å^{-3}$ | |

**Table 9.** Atomic coordinates ( x $10^4$) and equivalent isotropic displacement parameters ($Å^2$x $10^3$) for Pbca.res. U(eq) is defined as one third of the trace of the orthogonalized $U^{ij}$ tensor.

| | x | y | z | U(eq) |
|---|---|---|---|---|
| O(1) | 2067(1) | 1532(1) | 4210(1) | 66(1) |
| C(1) | 1914(1) | 806(2) | 5351(1) | 66(1) |
| C(2) | 1629(1) | 1753(2) | 4792(1) | 69(1) |
| C(3) | 2796(1) | 2102(2) | 4297(1) | 58(1) |
| C(4) | 3155(1) | 1435(1) | 4906(1) | 52(1) |
| C(5) | 3929(1) | 1470(2) | 4961(1) | 60(1) |
| C(6) | 4277(1) | 802(2) | 5474(1) | 66(1) |
| C(7) | 3877(1) | 52(2) | 5967(1) | 60(1) |
| C(8) | 4231(1) | -713(2) | 6488(1) | 81(1) |
| C(9) | 3840(1) | -1414(2) | 6963(1) | 100(1) |
| C(10) | 3075(1) | -1396(2) | 6944(1) | 100(1) |
| C(11) | 2710(1) | -682(2) | 6446(1) | 81(1) |
| C(12) | 3099(1) | 66(2) | 5938(1) | 58(1) |
| C(13) | 2741(1) | 787(1) | 5394(1) | 53(1) |
| C(14) | 845(1) | 1389(3) | 4608(1) | 104(1) |
| C(15) | 3215(1) | 1797(2) | 3668(1) | 58(1) |
| C(16) | 3380(1) | 361(2) | 3480(1) | 71(1) |
| C(17) | 3766(1) | 84(2) | 2907(1) | 82(1) |
| C(18) | 4006(1) | 1221(2) | 2503(1) | 77(1) |
| C(19) | 3838(1) | 2647(2) | 2696(1) | 92(1) |
| C(20) | 3448(1) | 2945(2) | 3267(1) | 79(1) |
| C(21) | 4435(1) | 913(3) | 1878(1) | 112(1) |

**Table 10.** Bond lengths [Å] and angles [°] for Pbca.res.

| | |
|---|---|
| O(1)-C(3) | 1.4307(16) |
| O(1)-C(2) | 1.4350(18) |
| C(1)-C(13) | 1.5057(19) |
| C(1)-C(2) | 1.505(2) |
| C(1)-H(1A) | 0.9700 |
| C(1)-H(1B) | 0.9700 |
| C(2)-C(14) | 1.508(2) |
| C(2)-H(2) | 0.9800 |
| C(3)-C(15) | 1.5091(19) |
| C(3)-C(4) | 1.5149(19) |
| C(3)-H(3) | 0.9800 |
| C(4)-C(13) | 1.3703(18) |
| C(4)-C(5) | 1.4130(19) |
| C(5)-C(6) | 1.354(2) |
| C(5)-H(5) | 0.9300 |
| C(6)-C(7) | 1.406(2) |
| C(6)-H(6) | 0.9300 |
| C(7)-C(8) | 1.413(2) |
| C(7)-C(12) | 1.416(2) |
| C(8)-C(9) | 1.349(3) |
| C(8)-H(8) | 0.9300 |
| C(9)-C(10) | 1.391(3) |
| C(9)-H(9) | 0.9300 |
| C(10)-C(11) | 1.365(2) |
| C(10)-H(10) | 0.9300 |
| C(11)-C(12) | 1.416(2) |
| C(11)-H(11) | 0.9300 |
| C(12)-C(13) | 1.4319(19) |
| C(14)-H(14A) | 0.9600 |
| C(14)-H(14B) | 0.9600 |
| C(14)-H(14C) | 0.9600 |
| C(15)-C(16) | 1.374(2) |
| C(15)-C(20) | 1.376(2) |
| C(16)-C(17) | 1.378(2) |

| | |
|---|---|
| C(16)-H(16) | 0.9300 |
| C(17)-C(18) | 1.377(2) |
| C(17)-H(17) | 0.9300 |
| C(18)-C(19) | 1.369(3) |
| C(18)-C(21) | 1.512(2) |
| C(19)-C(20) | 1.381(3) |
| C(19)-H(19) | 0.9300 |
| C(20)-H(20) | 0.9300 |
| C(21)-H(21A) | 0.9600 |
| C(21)-H(21B) | 0.9600 |
| C(21)-H(21C) | 0.9600 |

| | |
|---|---|
| C(3)-O(1)-C(2) | 111.40(11) |
| C(13)-C(1)-C(2) | 113.20(12) |
| C(13)-C(1)-H(1A) | 108.9 |
| C(2)-C(1)-H(1A) | 108.9 |
| C(13)-C(1)-H(1B) | 108.9 |
| C(2)-C(1)-H(1B) | 108.9 |
| H(1A)-C(1)-H(1B) | 107.8 |
| O(1)-C(2)-C(1) | 110.25(11) |
| O(1)-C(2)-C(14) | 107.00(14) |
| C(1)-C(2)-C(14) | 112.94(15) |
| O(1)-C(2)-H(2) | 108.9 |
| C(1)-C(2)-H(2) | 108.9 |
| C(14)-C(2)-H(2) | 108.9 |
| O(1)-C(3)-C(15) | 107.42(11) |
| O(1)-C(3)-C(4) | 111.01(11) |
| C(15)-C(3)-C(4) | 113.37(11) |
| O(1)-C(3)-H(3) | 108.3 |
| C(15)-C(3)-H(3) | 108.3 |
| C(4)-C(3)-H(3) | 108.3 |
| C(13)-C(4)-C(5) | 119.99(13) |
| C(13)-C(4)-C(3) | 121.00(12) |
| C(5)-C(4)-C(3) | 119.00(12) |
| C(6)-C(5)-C(4) | 121.09(13) |
| C(6)-C(5)-H(5) | 119.5 |

| | |
|---|---|
| C(4)-C(5)-H(5) | 119.5 |
| C(5)-C(6)-C(7) | 120.84(13) |
| C(5)-C(6)-H(6) | 119.6 |
| C(7)-C(6)-H(6) | 119.6 |
| C(6)-C(7)-C(8) | 121.68(15) |
| C(6)-C(7)-C(12) | 118.91(13) |
| C(8)-C(7)-C(12) | 119.41(14) |
| C(9)-C(8)-C(7) | 121.04(18) |
| C(9)-C(8)-H(8) | 119.5 |
| C(7)-C(8)-H(8) | 119.5 |
| C(8)-C(9)-C(10) | 120.18(18) |
| C(8)-C(9)-H(9) | 119.9 |
| C(10)-C(9)-H(9) | 119.9 |
| C(11)-C(10)-C(9) | 120.75(18) |
| C(11)-C(10)-H(10) | 119.6 |
| C(9)-C(10)-H(10) | 119.6 |
| C(10)-C(11)-C(12) | 120.98(17) |
| C(10)-C(11)-H(11) | 119.5 |
| C(12)-C(11)-H(11) | 119.5 |
| C(11)-C(12)-C(7) | 117.64(14) |
| C(11)-C(12)-C(13) | 123.00(14) |
| C(7)-C(12)-C(13) | 119.34(12) |
| C(4)-C(13)-C(12) | 119.66(12) |
| C(4)-C(13)-C(1) | 120.15(13) |
| C(12)-C(13)-C(1) | 120.18(12) |
| C(2)-C(14)-H(14A) | 109.5 |
| C(2)-C(14)-H(14B) | 109.5 |
| H(14A)-C(14)-H(14B) | 109.5 |
| C(2)-C(14)-H(14C) | 109.5 |
| H(14A)-C(14)-H(14C) | 109.5 |
| H(14B)-C(14)-H(14C) | 109.5 |
| C(16)-C(15)-C(20) | 118.01(14) |
| C(16)-C(15)-C(3) | 120.83(13) |
| C(20)-C(15)-C(3) | 121.15(13) |
| C(15)-C(16)-C(17) | 120.82(15) |
| C(15)-C(16)-H(16) | 119.6 |

| | |
|---|---|
| C(17)-C(16)-H(16) | 119.6 |
| C(16)-C(17)-C(18) | 121.80(16) |
| C(16)-C(17)-H(17) | 119.1 |
| C(18)-C(17)-H(17) | 119.1 |
| C(19)-C(18)-C(17) | 116.76(16) |
| C(19)-C(18)-C(21) | 121.61(19) |
| C(17)-C(18)-C(21) | 121.63(19) |
| C(18)-C(19)-C(20) | 122.21(17) |
| C(18)-C(19)-H(19) | 118.9 |
| C(20)-C(19)-H(19) | 118.9 |
| C(15)-C(20)-C(19) | 120.40(16) |
| C(15)-C(20)-H(20) | 119.8 |
| C(19)-C(20)-H(20) | 119.8 |
| C(18)-C(21)-H(21A) | 109.5 |
| C(18)-C(21)-H(21B) | 109.5 |
| H(21A)-C(21)-H(21B) | 109.5 |
| C(18)-C(21)-H(21C) | 109.5 |
| H(21A)-C(21)-H(21C) | 109.5 |
| H(21B)-C(21)-H(21C) | 109.5 |

Symmetry transformations used to generate equivalent atoms:

**Table 11.** Anisotropic displacement parameters ($Å^2 x\ 10^3$) for Pbca.res. The anisotropic displacement factor exponent takes the form: $-2\pi^2[\ h^2\ a^{*2}U^{11} + ...\ + 2\ h\ k\ a^*\ b^*\ U^{12}\ ]$.

| | $U^{11}$ | $U^{22}$ | $U^{33}$ | $U^{23}$ | $U^{13}$ | $U^{12}$ |
|---|---|---|---|---|---|---|
| O(1) | 55(1) | 68(1) | 74(1) | -9(1) | -8(1) | 7(1) |
| C(1) | 52(1) | 65(1) | 80(1) | -6(1) | 11(1) | 4(1) |
| C(2) | 54(1) | 66(1) | 87(1) | -13(1) | 1(1) | 15(1) |
| C(3) | 62(1) | 46(1) | 65(1) | -4(1) | -5(1) | 1(1) |
| C(4) | 52(1) | 46(1) | 57(1) | -9(1) | 2(1) | -1(1) |
| C(5) | 53(1) | 70(1) | 59(1) | -5(1) | 3(1) | -9(1) |
| C(6) | 49(1) | 80(1) | 68(1) | -12(1) | -2(1) | -3(1) |
| C(7) | 64(1) | 56(1) | 61(1) | -10(1) | -7(1) | 3(1) |
| C(8) | 85(1) | 74(1) | 85(1) | -1(1) | -24(1) | 3(1) |
| C(9) | 125(2) | 82(1) | 93(1) | 22(1) | -30(1) | -9(1) |
| C(10) | 125(2) | 90(1) | 84(1) | 28(1) | -1(1) | -16(1) |
| C(11) | 83(1) | 81(1) | 78(1) | 11(1) | 11(1) | -6(1) |
| C(12) | 64(1) | 52(1) | 59(1) | -5(1) | 5(1) | 2(1) |
| C(13) | 50(1) | 48(1) | 62(1) | -8(1) | 6(1) | 3(1) |
| C(14) | 54(1) | 128(2) | 130(2) | -12(1) | -7(1) | 20(1) |
| C(15) | 64(1) | 53(1) | 56(1) | 0(1) | -6(1) | -4(1) |
| C(16) | 86(1) | 56(1) | 69(1) | -4(1) | 13(1) | -11(1) |
| C(17) | 92(1) | 75(1) | 78(1) | -20(1) | 11(1) | -8(1) |
| C(18) | 68(1) | 107(1) | 57(1) | -1(1) | -4(1) | -9(1) |
| C(19) | 104(1) | 94(1) | 77(1) | 27(1) | 10(1) | -11(1) |
| C(20) | 100(1) | 61(1) | 77(1) | 11(1) | 1(1) | -2(1) |
| C(21) | 91(1) | 176(2) | 70(1) | -9(1) | 12(1) | -10(1) |

**Table 12.** Hydrogen coordinates ( x $10^4$) and isotropic displacement parameters ($Å^2$x $10^3$) for Pbca.res.

| | x | y | z | U(eq) |
|---|---|---|---|---|
| H(1A) | 1716 | 1179 | 5764 | 79 |
| H(1B) | 1739 | -209 | 5293 | 79 |
| H(2) | 1657 | 2806 | 4922 | 82 |
| H(3) | 2764 | 3186 | 4358 | 69 |
| H(5) | 4205 | 1960 | 4640 | 73 |
| H(6) | 4787 | 839 | 5500 | 79 |
| H(8) | 4742 | -734 | 6505 | 97 |
| H(9) | 4082 | -1910 | 7303 | 120 |
| H(10) | 2810 | -1876 | 7275 | 120 |
| H(11) | 2199 | -688 | 6440 | 97 |
| H(14A) | 692 | 2022 | 4251 | 156 |
| H(14B) | 532 | 1549 | 4983 | 156 |
| H(14C) | 814 | 363 | 4472 | 156 |
| H(16) | 3231 | -434 | 3744 | 85 |
| H(17) | 3866 | -899 | 2789 | 98 |
| H(19) | 3993 | 3441 | 2435 | 110 |
| H(20) | 3342 | 3928 | 3381 | 95 |
| H(21A) | 4428 | -139 | 1786 | 168 |
| H(21B) | 4934 | 1237 | 1935 | 168 |
| H(21C) | 4216 | 1444 | 1516 | 168 |

**Table 13.** Torsion angles [°] for Pbca.res.

| | |
|---|---|
| C(3)-O(1)-C(2)-C(1) | -67.27(15) |
| C(3)-O(1)-C(2)-C(14) | 169.55(13) |
| C(13)-C(1)-C(2)-O(1) | 41.55(17) |
| C(13)-C(1)-C(2)-C(14) | 161.19(14) |
| C(2)-O(1)-C(3)-C(15) | 179.10(11) |
| C(2)-O(1)-C(3)-C(4) | 54.64(14) |
| O(1)-C(3)-C(4)-C(13) | -19.18(17) |
| C(15)-C(3)-C(4)-C(13) | -140.20(12) |
| O(1)-C(3)-C(4)-C(5) | 159.93(11) |
| C(15)-C(3)-C(4)-C(5) | 38.91(17) |
| C(13)-C(4)-C(5)-C(6) | 3.5(2) |
| C(3)-C(4)-C(5)-C(6) | -175.60(12) |
| C(4)-C(5)-C(6)-C(7) | 0.0(2) |
| C(5)-C(6)-C(7)-C(8) | 176.87(14) |
| C(5)-C(6)-C(7)-C(12) | -3.0(2) |
| C(6)-C(7)-C(8)-C(9) | 179.25(16) |
| C(12)-C(7)-C(8)-C(9) | -0.9(2) |
| C(7)-C(8)-C(9)-C(10) | 0.2(3) |
| C(8)-C(9)-C(10)-C(11) | 0.5(3) |
| C(9)-C(10)-C(11)-C(12) | -0.4(3) |
| C(10)-C(11)-C(12)-C(7) | -0.2(2) |
| C(10)-C(11)-C(12)-C(13) | 177.86(16) |
| C(6)-C(7)-C(12)-C(11) | -179.24(14) |
| C(8)-C(7)-C(12)-C(11) | 0.9(2) |
| C(6)-C(7)-C(12)-C(13) | 2.59(19) |
| C(8)-C(7)-C(12)-C(13) | -177.30(13) |
| C(5)-C(4)-C(13)-C(12) | -3.86(18) |
| C(3)-C(4)-C(13)-C(12) | 175.24(11) |
| C(5)-C(4)-C(13)-C(1) | 177.40(12) |
| C(3)-C(4)-C(13)-C(1) | -3.50(18) |
| C(11)-C(12)-C(13)-C(4) | -177.23(13) |
| C(7)-C(12)-C(13)-C(4) | 0.84(19) |
| C(11)-C(12)-C(13)-C(1) | 1.5(2) |
| C(7)-C(12)-C(13)-C(1) | 179.58(12) |

| | |
|---|---|
| C(2)-C(1)-C(13)-C(4) | -7.74(19) |
| C(2)-C(1)-C(13)-C(12) | 173.53(12) |
| O(1)-C(3)-C(15)-C(16) | -67.16(17) |
| C(4)-C(3)-C(15)-C(16) | 55.86(18) |
| O(1)-C(3)-C(15)-C(20) | 113.39(15) |
| C(4)-C(3)-C(15)-C(20) | -123.59(15) |
| C(20)-C(15)-C(16)-C(17) | -0.3(2) |
| C(3)-C(15)-C(16)-C(17) | -179.74(15) |
| C(15)-C(16)-C(17)-C(18) | 0.6(3) |
| C(16)-C(17)-C(18)-C(19) | -0.5(3) |
| C(16)-C(17)-C(18)-C(21) | 179.31(17) |
| C(17)-C(18)-C(19)-C(20) | 0.0(3) |
| C(21)-C(18)-C(19)-C(20) | -179.81(17) |
| C(16)-C(15)-C(20)-C(19) | -0.2(3) |
| C(3)-C(15)-C(20)-C(19) | 179.24(15) |
| C(18)-C(19)-C(20)-C(15) | 0.4(3) |

Symmetry transformations used to generate equivalent atoms:

**Table 14.** Hydrogen bonds for Pbca.res [Å and °].

| D-H...A | d(D-H) | d(H...A) | d(D...A) | <(DHA) |
|---|---|---|---|---|